ADDRESS OF THE ORGANIZING COMMITTEE

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Editorial Note:
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BULGARIAN SOCIETY OF BIOMEDICAL PHYSICS AND ENGINEERING
Dear Participants,

At the 12-th NATIONAL MEDICAL PHYSICS AND BIOMEDICAL ENGINEERING CONFERENCE-NMPEC-2016 with international participation, on behalf of the Organizing Committee and the BSBPE Board, we are pleased to cordially welcome you to this scientific forum which will be held at the Inter Expo Center, Sofia.

Co-organizers of this significant event are the Nuclear Regulatory Agency of Bulgaria, the Union of Physicists in Bulgaria, the Bulgarian Association of Radiology and the Bulgarian Biochemical, Biophysical and Molecular Biology Society.

The NMPEC-2016 conference is endorsed and supported by the International Organization for Medical Physics (IOMP) and the European Federation of Organizations for Medical Physics (EFOMP). Support letters from the Croatian Medical and Biological Engineering Society (CROMBES), the Hungarian Society of Medical Physicists (HSMP) and the Hellenic Association of Medical Physicists (HAMP) were received as well.

This is the major conference in the area of Medical Physics and Biomedical Engineering in Bulgaria and we received more than 70 abstracts from participants from our and other countries. Through the exchange of ideas and discussions on state-of-the-art knowledge, on topics of education and training of specialists in this branch of science and technology, as well as on problems to be solved, the NMPEC-2016 is expected to stimulate further research in this dynamic field.

NMPEC-2016 will feature plenary talks by world-renowned experts, a variety of sessions focused on the most pressing issues in medical and non-medical use of sophisticated technology, health care concerns and regulations associated with ionizing and non-ionizing radiation, biophysical phenomena and engineering progress and applications.

NMPEC-2016 will assist the development and strengthening of international scientific and personal contacts and cooperation. During the Conference, students will have the opportunity to present their work and to demonstrate their skills in communicating and networking with the Medical Physics, Biophysics and Biomedical Engineering communities.

The NMPEC-2016 conference marks the 45th Anniversary of BSBPE, a remarkable event that will be noted in a special session at the conference dinner.

We would like to express our sincere thanks to all sponsors and collaborators who supported the conference and helped its organization.

The Organizing Committee and the BSBPE Board are particularly honored to welcome all of you to NMPEC-2016 and the wonderful city of Sofia, and to wish you pleasant stay and fruitful work.

Professor Boris Tenchov, PhD, DSc
Member of the Bulgarian Acad Sci
President of BSBPE

Assistant Professor Lubomir Traikov, PhD
Chair of Organizing Committee of NMPEC-2016
Organized by: Bulgarian Society of Biomedical Physics and Engineering

Endorsed by: International Organization for Medical Physics
And: European Federation of Organizations for Medical Physics

Co-organizers: Nuclear Regulatory Agency
Union of Physicists in Bulgaria Bulgarian Association of Radiology

And: Bulgarian Biochemical, Biophysical and Molecular Biology Society

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<table>
<thead>
<tr>
<th>Time</th>
<th>Session</th>
<th>Name</th>
<th>Place/Hall</th>
</tr>
</thead>
<tbody>
<tr>
<td>10:00-18:00</td>
<td>Registration</td>
<td></td>
<td>Registration desk</td>
</tr>
<tr>
<td>13:30-14:00</td>
<td>Opening ceremony</td>
<td></td>
<td>Musala</td>
</tr>
<tr>
<td>14:00-15:30</td>
<td>Session Radiology and Roentgenology 1</td>
<td>Chair Professor Boris Tenchov, President of BSBPE</td>
<td>Musala</td>
</tr>
<tr>
<td>14:00-14:45</td>
<td>PL1</td>
<td>Slavik Tabakov “Medical Imaging Equipment – 50 years of progress, related education, impact on medicine and current trends”</td>
<td>Musala</td>
</tr>
<tr>
<td>14:45-15:00</td>
<td>O1-1</td>
<td>Peter Trindev “60 years from the invention of Anger gamma camera”</td>
<td>Musala</td>
</tr>
<tr>
<td>15:00-15:15</td>
<td>O1-2</td>
<td>Simona Avramova-Cholakova, D. Kostova-Lefterova “Pilot study of patient doses from digital breast tomosynthesis in Bulgaria”</td>
<td>Musala</td>
</tr>
<tr>
<td>15:30-16:00</td>
<td>Coffee Break</td>
<td></td>
<td>Vihren</td>
</tr>
<tr>
<td>16:00-17:30</td>
<td>Session Biomedical Engineering</td>
<td>Chair Professor Virginia Tsapaki, Secretary General of IOMP</td>
<td>Musala</td>
</tr>
<tr>
<td>16:00-16:30</td>
<td>PL2</td>
<td>Giovanni Bortolan, I. Simova, I. Gruev, I. Christov, S. Georgieva “Comparative study of T-wave alternans in elderly and young competitive athletes”</td>
<td>Musala</td>
</tr>
<tr>
<td>16:30-16:45</td>
<td>O2-1</td>
<td>J. Przondziono, W. Walke, J. Szala, J. Wieczorek “Ultrasound imaging: signal acquisition, new advanced processing for biomedical and industrial applications”</td>
<td>Musala</td>
</tr>
<tr>
<td>16:45-17:00</td>
<td>O2-2</td>
<td>Lubomir Traikov, A. Dzambazova, R. Hadjiolova, V. Velchev, D. Vasilev, J.Petrova “Complex analysis of asymptomatic carotid stenosis and restenosis-according parameters- ABI, FMD and IMT of human carotid arteries-restenosis as a consequence of the local strain stress”</td>
<td>Musala</td>
</tr>
<tr>
<td>17:00-17:15</td>
<td>O2-3</td>
<td>Ivan Tsanev, A. Dimov, G. Kasparyan “National Database for Patient Dose Registration and Analysis in Diagnostic Radiology”</td>
<td>Musala</td>
</tr>
<tr>
<td>17:15-17:30</td>
<td>O2-4</td>
<td>Sergey Podtaev, N. Zubareva, A. Parshakov, E. Smirnova “Detection of Endothelial Dysfunction Using Skin Temperature Oscillations Analysis”</td>
<td>Musala</td>
</tr>
<tr>
<td>Time</td>
<td>Session</td>
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<tr>
<td>09:00-18:00</td>
<td>Registration</td>
<td></td>
<td>Registration desk</td>
</tr>
<tr>
<td>09:00-10:30</td>
<td>Session Radiology and Roentgenology 2</td>
<td>Chair  Professor Slavik Tabakov, President of IOMP</td>
<td>Musala</td>
</tr>
<tr>
<td>09:00-09:30</td>
<td>PL3</td>
<td>Virginia Tsapaki  “Incidents and accidents in imaging departments. What’s next?”</td>
<td>Musala</td>
</tr>
<tr>
<td>09:30-09:45</td>
<td>O3-1</td>
<td>Pavlina Pike, L. Johnson “Strategies for minimizing patient radiation dose in interventional fluoroscopy”</td>
<td>Musala</td>
</tr>
<tr>
<td>09:45-10:00</td>
<td>O3-2</td>
<td>M. Dimcheva,  Peter Trindev  “National survey on the accuracy of dose calibrations”</td>
<td>Musala</td>
</tr>
<tr>
<td>10:00-10:15</td>
<td>O3-3</td>
<td>Kristina Bliznakova, I. Buliev, Z. Bliznakov  “Education and training related to anthropomorphic phantoms for medical physics experts”</td>
<td>Musala</td>
</tr>
<tr>
<td>10:15-10:30</td>
<td>O3-4</td>
<td>Desislava Kostova-Lefterova, F. Simeonov, D. Ivanova “Tracking the effect of optimisation in a paediatric radiology department”</td>
<td>Musala</td>
</tr>
<tr>
<td>10:30-11:00</td>
<td>Coffee Break</td>
<td></td>
<td>Vihren</td>
</tr>
<tr>
<td>11:00-13:00</td>
<td>Session Biophysics</td>
<td>Chair  Assist. Prof. Lubomir Traikov, Chairman of Organizing Committee</td>
<td>Musala</td>
</tr>
<tr>
<td>11:00-11:30</td>
<td>PL4</td>
<td>Boris Tenchov  “Nanotechnologies in gene therapy – non-viral vectors for nucleic acid delivery”</td>
<td>Musala</td>
</tr>
<tr>
<td>11:30-11:45</td>
<td>O4-1</td>
<td>Roxana Popescu, A.I. Apostol, E. A. Andronescu, M. Grumezescu, D. Savu “Fabrication of functionalized magnetite nanoparticles with applications in drug delivery systems”</td>
<td>Musala</td>
</tr>
<tr>
<td>11:45-12:00</td>
<td>O4-2</td>
<td>Miroslav Karabaliev, B. Tacheva  “Electrochemical approach to investigate drug-nanoparticles interactions”</td>
<td>Musala</td>
</tr>
<tr>
<td>12:00-12:15</td>
<td>O4-3</td>
<td>Rositsa Marinova, P. Petkov, L. Litov  “CG molecular dynamics study of indolicidin in water solution”</td>
<td>Musala</td>
</tr>
<tr>
<td>12:15-12:30</td>
<td>O4-4</td>
<td>Virginia Doltchinkova, P. Angelova, S. Petrova  “Vipoxin effects on the surface electrical properties and membrane transport of protons in human erythrocytes”</td>
<td>Musala</td>
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<tr>
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<tr>
<td>12:30-12:45</td>
<td>O4-5</td>
<td><strong>Alexander G. Dimitrov</strong> “Transformation of phenomenological models of sodium-potassium pump into biophysically based ones”</td>
<td>Musala</td>
</tr>
<tr>
<td>12:45-13:00</td>
<td>O4-6</td>
<td><strong>Andrey Popatanasov, A. Trifonov</strong> “Modification with short laser pulses of collagen derived matrices crosslinked with D-fructose for potential use in the regenerative medicine”</td>
<td>Musala</td>
</tr>
<tr>
<td>13:00-14:00</td>
<td></td>
<td><strong>Lunch time</strong></td>
<td></td>
</tr>
<tr>
<td>14:00-16:00</td>
<td>RT</td>
<td><strong>Round Table Discussion</strong> – Problems of Education in Bulgaria (dedicated to the 4th International Day of Medical Physics) EDUCATION IN MEDICAL PHYSICS: THE KEY TO SUCCESS</td>
<td>Musala</td>
</tr>
<tr>
<td></td>
<td></td>
<td><strong>Moderators:</strong> <strong>Professor Athanas Kristev</strong>, Secretary General of Medical University-Plovdiv, Dept. Medical Physics and Biophysics, <strong>Assoc. Professor Leander Litov</strong>, Sofia University “St. Kliment Ohridski”, Faculty of Physics</td>
<td></td>
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<tr>
<td>16:00-16:30</td>
<td></td>
<td><strong>Coffee Break</strong></td>
<td>Vihren</td>
</tr>
<tr>
<td>16:30-18:30</td>
<td></td>
<td><strong>BSBPE members meeting</strong></td>
<td>Musala</td>
</tr>
<tr>
<td>19:00-</td>
<td></td>
<td><strong>Conference Dinner and BSBPE 45th Anniversary Meeting</strong></td>
<td>Panorama</td>
</tr>
</tbody>
</table>

### Saturday, November 5

<table>
<thead>
<tr>
<th>Time</th>
<th>Session</th>
<th>Name</th>
<th>Place/Hall</th>
</tr>
</thead>
<tbody>
<tr>
<td>09:00-11:00</td>
<td></td>
<td><strong>Session Radiology and Roentgenology 3</strong> Chair Assoc. Prof. Peter Trindev, Past President of BSBPE</td>
<td>Musala</td>
</tr>
<tr>
<td>09:00-09:15</td>
<td>PL5</td>
<td><strong>Slavik Tabakov</strong> “MTF and Contrast Inversion”</td>
<td>Musala</td>
</tr>
<tr>
<td>09:15-09:30</td>
<td>O5-1</td>
<td><strong>Pavlina Pike, L. Johnson</strong> “CT dose optimization and tracking across multiple facilities”</td>
<td>Musala</td>
</tr>
<tr>
<td>09:30-09:45</td>
<td>O5-2</td>
<td><strong>Simona Avramova-Cholakova, E. Petrova, S. Shalamanov, I. Dyakov</strong> “Radiation exposure of patients from whole body examinations on new PET-CT system”</td>
<td>Musala</td>
</tr>
<tr>
<td>09:45-10:00</td>
<td>O5-3</td>
<td><strong>Simona Avramova-Cholakova, E. Petrova, S. Shalamanov, I. Dyakov</strong> “Radiation exposure of patients from two procedures on new SPECT-CT system”</td>
<td>Musala</td>
</tr>
<tr>
<td>10:00-10:15</td>
<td>O5-4</td>
<td><strong>Desislava Kostova-Lefterova, V. Hadzhiyska, Sh. Masso, F. Vasileva</strong> “Survey of practice and dose optimisation strategies in paediatric PET/CT procedures”</td>
<td>Musala</td>
</tr>
<tr>
<td>10:15-10:30</td>
<td>O5-5</td>
<td><strong>Nely Gesheva-Atanasova, D. Stoeva</strong> “Comparison of 3D conformal radiotherapy and helical tomotherapy for irradiation of the breast and regional lymphatic”</td>
<td>Musala</td>
</tr>
<tr>
<td>10:30-11:00</td>
<td>O5-6</td>
<td><strong>Nadir Küçük</strong> “Evaluation of SRS/SBRT Treatment using Dosimetric Metrics”</td>
<td>Musala</td>
</tr>
<tr>
<td>11:00-11:30</td>
<td></td>
<td><strong>Coffee Break</strong></td>
<td>Vihren</td>
</tr>
<tr>
<td>Time</td>
<td>Session Non-Ionizing Radiation</td>
<td>Chair Assoc. Prof. Michaela Ivanova, National Center of Public Health Protection and Analysis Sofia</td>
<td>Musala</td>
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<td>-------------------</td>
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</tr>
<tr>
<td>11:30-12:00</td>
<td>PL6 Marko S. Markov “Bulgarian contribution in electromagnetic biology and medicine”</td>
<td>Musala</td>
<td></td>
</tr>
<tr>
<td>12:00-12:15</td>
<td>O6-1 Nikolai Atanasov, G. Atanasova, L.Traikov, M. Kouzmanova, M. Markov, L.Veselinova, A. Stefanov “Evaluation of a microwave system for hyperthermia treatment of cancer in animals”</td>
<td>Musala</td>
<td></td>
</tr>
<tr>
<td>12:15-12:30</td>
<td>O6-2 Petia Ivanova, M. Israel “Data from the national noise measuring system in the urbanized regions of Bulgaria”</td>
<td>Musala</td>
<td></td>
</tr>
<tr>
<td>12:30-12:45</td>
<td>O6-3 Emil Georgiev, T. Marov, V. Ivanov, G. Kirova “Development of magnetic resonance imaging phantom for tissue selective techniques”</td>
<td>Musala</td>
<td></td>
</tr>
<tr>
<td>12:45-13:00</td>
<td>O6-4 J. Ryaby, Marko Markov “Electromagnetic stimulation in musculoskeletal tissue repair”</td>
<td>Musala</td>
<td></td>
</tr>
<tr>
<td>13:00-13:15</td>
<td>NMPEC-2016 Closing ceremony</td>
<td></td>
<td></td>
</tr>
<tr>
<td>15:30-18:30</td>
<td>Sightseeing tour Sofia and surroundings</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**POSTERS**

**Poster Session Ionizing and Non-Ionizing Radiation**

P01 Dimov A., Kasparyan G., Tsanev I., Vassileva F. “Application of EFOMP and EUREF Quality Control protocols in evaluation of a modern full field digital mammography system”

P02 Gancheva M., Krastev B., Gesheva–Atanasova N. “Evaluation the feasibility of VMAT treatment plan verification with Octavius 4D phantom using different dosimetry criteria”

P03 Ivanova N., Chaushev B., Ivanova S. “Life in radiation”

P04 Ivanov L. “Dose-Area product meter with extended functionality”

P05 Ivanov L. “Active ionizing chamber with analog and digital mode of operation”

P06 Ivanov L. “Variable packet length protocol (VPL protocol) for real time data transmission”

P07 Shalamanova Ts., Topalova Iv. “Analysis and evaluation of electromagnetic exposure in urban area with high density of sources”

**Poster Session Biophysics**

P08 Abarova S., Koyanova R., Traikov L., Tancheva L., Tenchev B. “Protectant Drug Efficacy Against Scopolamine-Induced Dementia In Mice, A DSC Approach”

P09 Alexandrov S. A., Todorov R. K., Exerowa D. R. “The role of Ca\(^{2+}\) on stability of foam films from lysophosphatidylcholine and Curosurf”

P10 Al Sharif M., Alov P., Tsakovska I., Pajeva I. „Pharmacophore modeling of PPAR\(\gamma\) partial agonist”

P11 Bangyoza M., Jordanova A., Tsanova A., Stoyanova V., Stoimenova E., Christova E., Lalchev Z. “Methods of diagnostic of neonatal respiratory distress syndrome based on gastric aspirates samples in order to appropriate therapy”
Preface

The human body is a set of dynamical processes based on biophysical systems that work together in a certain rhythm and harmony. Any distraction to this coherent rhythm might result in a misbalance of structural and functional dynamics in living system and can triggered a set of pathological processes. These pathological processes can lead to ultimate termination of the functions of the whole body.

Studying the biophysical properties of the human body from one side and influence of environmental physical factors from other side is one complex task on the way of generation of new theoretic mechanisms of auto regulation in living systems and possible pathways of interaction of external environmental factors with living systems.

Nowadays medical nanotechnologies developing of an early diagnostic and therapeutic facilities made available via Medical Physics will help us to maintain a better quality of life for human beings.

Gathering of specialists from all over the country and the world to initiate and to create a creative environment for discussion and the formation of opinions on important issues of biomedical physics, biophysics and biomedical engineering in the Republic of Bulgaria is the importance of NMPEC-2016.

The conference was held at International Expo Center-IEC, Sofia, Bulgaria.

According registration list 125 active members take place in this conference and around 100 attend as a passive members. At NMPEC-2016 conference were presented 25 countries. Albania, Armenia, Austria, Croatia, Cyprus, Italy, India, Germany, Greece, Japan, Luxemburg, Macedonia, Malta, Moldova, Montenegro, Poland, Romania, Russia, Serbia, Slovenia, Sweden, Switzerland, Turkey, Ukraine, UK, and USA.

In this conference were delivered 6 plenary talks and 27 Oral reports divided in 6 sessions. The poster session include 31 posters with various topics of biomedical physics, biophysics and biomedical engineering.

The title and chairpersons of the sessions are as follow:

1. Session Radiology and Roentgenology 1- Chair Professor Boris Tenchov, President of BSBPE
2. Session Biomedical Engineering- Chair Professor Virginia Tsapaki, Secretary General of IOMP
3. Session Radiology and Roentgenology 2- Chair Professor Slavik Tabakov, President of IOMP
4. Session Biophysics- Chair Assist. Prof. Lubomir Traikov, Chairman of Organizing Committee
5. Session Radiology and Roentgenology 3- Chair Assoc. Prof. Peter Trindev, Past President of BSBPE
6. Session Non-Ionizing Radiation- Chair Assoc. Prof. Michaela Ivanova, National Center of Public Health Protection and Analysis Sofia

The present Proceedings by the NMPEC-2016 conference brings together plenary and poster reports of bio-medical science specialists from all over the country and the rest of the world. Reports in the current proceedings NMPEC-2016 include the fundamental principles of physical interactions between molecules and cells with environmental factors, the interactions of biological matter with ionizing and non-ionizing radiation as well as their Dosimetry and the development of engineering methods for gathering and processing bio-medical signals.
Biomedical physics, biophysics and engineering cover a broad range of disciplines that apply quantitative physical methods to the study of fundamental biological problems as well as the more practical concerns of human physiology, disease, and medical diagnosis and treatment.

One of the challenges facing modern bio-medical science is the need for a more physical understanding of biological functions, particularly the protein-protein interactions.

Modern physics tools are ideally suited to probing protein function at the level of single molecules or small complexes. By combining a variety of measurement techniques and studies of both proteins and membranes, we will come to an understanding of the cell as a complex highly ordered machine. This advance is of fundamental scientific importance and will be directly applicable to medicine.

In the area of bio-medical physics and engineering a few of the topics that exploit physics and physical methods are the interactions of light, ionizing radiation, non-ionizing radiation such as microwaves, with living tissues. Dosimetry, diagnostic and therapeutic techniques such as X-ray, gamma ray and NMR computer tomography, diagnostic ultrasound and radiation therapy that dominate modern medicine.

It is evident from this partial list that a strong national program in medical physics is essential for republic of Bulgaria to be in the forefront in basic medical science and in medical diagnostics and therapeutics.

Delivery of high-quality medical care requires a large pool of highly-trained individuals who will function in hospitals and other health care delivery settings. Medical diagnostic and therapeutic equipment in republic of Bulgaria plays a major role, for taking a lifesaving decisions in clinical practice. Therefore there is a consistently strong demand for well-trained physicists with special expertise in this area.

Editorial Board of NMPEC-2016 Proceedings

Professor Boris Tenchov, PhD, DSc.
Assistant professor Lubomir Traikov, PhD.
Associated Professor Athanas Slavchev, PhD.
Assistant professor Todor Bogdanov, PhD.
Assistant professor Silvia Abarova, PhD.
## CONTENT

### Preface

<table>
<thead>
<tr>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>10</td>
</tr>
</tbody>
</table>

### Session Radiology and Roentgenology 1

| Slavik Tabakov “Medical Imaging Equipment – 50 years of progress, related education, impact on medicine and current trends” | 16 |
| Peter Trindev “60 years from the invention of Anger gamma camera” | 17 |
| Anna Zagorska, Ts. Tsrunchev, Z. Buchacliev, P. Arsova, J. Vassileva “Development of a new TLD holder for eye lens dosimetry in interventional radiology” | 18 |

### Session Biomedical Engineering

| Giovanni Bortolan, I. Simova, I. Gruev, I. Christov, S. Georgieva “Comparative study of T-wave alternans in elderly and young competitive athletes” | 30 |
| J. Przondziono, W. Walke, J. Szala, J. Wieczorek “Ultrasound imaging: signal acquisition, new advanced processing for biomedical and industrial applications” | 43 |
| Lubomir Traikov, A. Dzambazova, R. Hadjiolova, V. Velchev, D. Vasilev, J. Petrova “Complex analysis of asymptomatic carotid stenosis and restenosis-according parameters- ABI, FMD and IMT of human carotid arteries-restenosis as a consequence of the local strain stress” | 44 |
| Ivan Tsanev, A. Dimov, G. Kasparyan “National Database for Patient Dose Registration and Analysis in Diagnostic Radiology” | 51 |
| Sergey Podtatev, N. Zubareva, A. Parshakov, E. Smirnova “Detection of Endothelial Dysfunction Using Skin Temperature Oscillations Analysis” | 61 |

### Session Radiology and Roentgenology 2

| M. Dimcheva, Peter Trindev “National survey on the accuracy of dose calibrations” | 64 |
| Virginia Tsapaki “Incidents and accidents in imaging departments. What’s next?” | 70 |
| Desislava Kostova-Lefterova, F. Simeonov, D. Ivanova “Tracking the effect of optimisation in a paediatric radiology department” | 71 |
| Simona Avramova-Cholakova, D. Kostova-Lefterova “Pilot study of patient doses from digital breast tomosynthesis in Bulgaria” | 77 |
**Session Biophysics**

Boris Tenchov “Nanotechnologies in gene therapy – non-viral vectors for nucleic acid delivery” 96

Roxana Popescu, A.I. Apostol, E. A. Andronescu, M. Grumezescu, D. Savu “Fabrication of functionalized magnetite nanoparticles with applications in drug delivery systems” 97

Miroslav Karabaliev, B. Tacheva “Electrochemical approach to investigate drug-nanoparticles interactions” 98

Rositsa Marinova, P. Petkov, L. Litov “CG molecular dynamics study of indolicidin in water solution” 106

Virginia Doltchinkova, P. Angelova, S. Petrova “Vipoxin effects on the surface electrical properties and membrane transport of protons in human erythrocytes” 107

Alexander G. Dimitrov “Transformation of phenomenological models of sodium-potassium pump into biophysically based ones” 108

Andrey Popatanasov, A. Trifonov “Modification with short laser pulses of collagen derived matrices crosslinked with D-fructose for potential use in the regenerative medicine” 116

**Session Radiology and Roentgenology 3**

Simona Avramova-Cholakova, E. Petrova, S. Shalamanov, I. Dyakov “Radiation exposure of patients from two procedures on new SPECT-CT system” 117

Simona Avramova-Cholakova, E. Petrova, S. Shalamanov, I. Dyakov “Radiation exposure of patients from whole body examinations on new PET-CT system” 126

Desislava Kostova-Lefterova, V. Hadzhiyska, Sh. Masso, F. Vasileva “Survey of practice and dose optimisation strategies in paediatric PET/CT procedures” 135

Slavik Tabakov “MTF and Contrast Inversion” 145

Kristina Bliznakova, I. Buliev, Z. Bliznakov “Education and training related to anthropomorphic phantoms for medical physics experts”” 146

Pavlina Pike, L. Johnson “CT dose optimization and tracking across multiple facilities 147

Pavlina Pike, L. Johnson “Strategies for minimizing patient radiation dose in interventional fluoroscopy” 148

Nely Gesheva-Atanasova, D. Stoeva “Comparison of 3D conformal radiotherapy and helical tomotherapy for irradiation of the breast and regional lymphatic” 149

**Session Non-Ionizing Radiation**

Petia Ivanova, M. Israel “Data from the national noise measuring system in the urbanized regions of Bulgaria” 151
Various reports

Dimov A., Kasparyan G., Tsanev I., Vassileva F. “Application of EFOMP and EUREF Quality Control protocols in evaluation of a modern full field digital mammography system” 160

Gancheva M., Krastev B., Gesheva–Atanasova N. “Evaluation the feasibility of VMAT treatment plan verification with Octavius 4D phantom using different dosimetry criteria” 167

Ivanova N., Chaushev B., Ivanova S. “Life in radiation” 168

Ivanov L. “Dose-Area product meter with extended functionality” 179

Ivanov L. “Active ionizing chamber with analog and digital mode of operation” 180

Ivanov L. “Variable packet length protocol (VPL protocol) for real time data transmission” 181

Shalamanova Ts., Topalova Iv. “Analysis and evaluation of electromagnetic exposure in urban area with high density of sources” 183

Zaharinoiva S., Abarova S., Tanechev L., Stoeva S., Paypanova T., Koynova R., Tenchov B. "Effects of synthetic neuropeptides (neurotensins) on drug-induced neurodegenerative disorders" 192

Radeva D., Dimitrova St., Pavlova B., Paunov M., Kouzmanova M., Dankov K., Tsonev Ts., Velikova V., Goltsev V. “Plant health estimation using prompt chlorophyll a fluorescence imaging in leaves of two varieties of bean plants” 198

Alexandrov S. A., Todorov R. K., Exerowa D. R. “The role of Ca$^{2+}$ on stability of foam films from lysophosphatidylcholine and CUROSURF” 213

Al Sharif M., Alov P., Tsakovska I., Pajeva I. „Pharmacophore modeling of PPAR $\gamma$ partial agonist” 221

Bangyozova M., Jordanova A., Tsanova A., Stoyanova V., Stoimenova E., Christeva E., Lalchev Z. “Methods of diagnostic of neonatal respiratory distress syndrome based on gastric aspirates samples in order to appropriate therapy” 222


Djenev I. “Investigation of the influence of the endotoxin on the deformability of red blood cells in vitro” 224

Vladkova R. “Ordering of the numerous cytochrome $bc_1$ X-ray crystal structure in a sequence of events during substrate processing in the $Q_0$ site of the complex” 225

Chakalov I., Ivanova P., Traikov L. “Estimation of biomechanical force of action as a function of three different chewing forces studied by image densitometry analysis” 241

Ilieva D. “Temperature-dependent, spatial and temporal controlled azobenzene polymeric materials” 252


Nikola A., Keranov I., Michel M., Vladkova T., Kostadinova A. “Characterisation and biological response of electrospun amphiphilic poly (Dimethylsiloxane-B-acrylic Acid) fibrous scaffolds” 254


Popatnasov A. “A low-cost differential thermal analysis (DTA) apparatus for measuring the thermal properties and behavior of protein and carbohydrate-based hydrogels” 256

Zaytseva E., Deperas-Kaminska M., Kutsalo P., Mitsyn G., Molokanov A., Gaevsky V., Wojcik A. “Cytogenetic radio-sensitivity of human peripheral blood lymphocytes to protons and gamma rays” 257


Semkova S., Nikolova B., Murayama S., Stoyanova E., Tsoneva I., Zhelev Zh., Aoki I., R. Bakalova “Visualization of passive and electro-assisted delivery of quantum dot-labeled nanoparticles in vitro and in vivo using fluorescent and magnetic resonance imaging” 280

Zasheva A., Abarova S., Tenchov B. “Corticosteroid interactions with human serum albumin” 281

Sezanova B., Antonova B., Naidenov E., Tenchov B. “Changes in the state of the plasma proteome and cerebrospinal fluid in Glioblastoma multiforme” 282

Stoichev S., Andreeva T., Taneva S., Krastev R. “Optimization of polyelectrolyte multilayer coatings for biofunctionalization of cardiovascular stents by incorporation of graphene oxide” 283

Vassilev P., Tashev R., Ardasheva R., Prissadova N., Slavchev V., Turiyski V., Kristev A. “Combined in vivo and in vitro biophysical methods for investigation of abdominal hypertensive rats” 284

Abarova S., Koynova R., Traikov L., Tanecheva L., Tenchov B. “Protectant Drug Efficacy Against Scopolamine-Induced Dementia In Mice, A DSC Approach” 289

Mancheva K., Stephanova D.I., Wolf W., Kossev A. “The effect of co-activation of antagonist muscles on recruitment curve during transcranial magnetic stimulation” 290

Marko S. Markov “Bulgarian contribution in electromagnetic biology and medicine” 303

Marko S. Markov “Dosimetry in Bioelectromagnetics” 304

Emil Georgiev, T. Marov, V. Ivanov, G. Kirova “Development of magnetic resonance imaging phantom for tissue selective techniques” 305

AUTHORS INDEX

Sponsors list
Session
Radiology and Roentgenology 1
MEDICAL IMAGING EQUIPMENT – 50 YEARS OF PROGRESS, RELATED EDUCATION, IMPACT ON MEDICINE AND CURRENT TRENDS

S. Tabakov, President IOMP 1,2

1King’s College London, UK; 2International Organization for Medical Physics, www.iomp.org

The rapid development of medical imaging equipment in the past 50 years led to significant changes in contemporary medical diagnostics. The presentation gives an overview of the invention of the new medical imaging equipment and their implementation in clinical practice. Special place is devoted to the medical physicists, engineers and other specialists, who invented various imaging modalities in the field of X-ray imaging, CT scanning, Nuclear Medicine, Magnetic Resonance and Ultrasound Imaging. Their pioneering work is given in chronological order, showing the development of ideas and their evolution as knowledge transfer from one field to another.

The need of new type of medical physics/engineering education, related to this revolutionary equipment development, is underlined. This includes the introduction of e-learning in the profession, the pioneering of the first e-Encyclopaedia and Dictionary of Medical Physics and other innovative educational development. Their role is highlighted as some of the main supporters for the professional growth in the past 20 years.

The digitalisation of medical imaging is described as contributor to both- the increased image quality and the introduction of quantitative imaging. Methods based on extraction of new information from medical imaging, as well as mathematical modelling, based on imaging, are shown as some of the future trends in the progress in medical imaging.

The presentation emphasizes medical physics and engineering as a significant driving force for contemporary imaging diagnostics.

- **Key words:** medical physics professional issues, medical physics education
60 YEARS FROM THE INVENTION OF ANGER GAMMA CAMERA

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QC consultant, Sofia, Bulgaria

It is not possible to predict what would look like today the nuclear medicine diagnostic without the genius invention of Hal Anger 60 years ago. Development of modern detectors of ionizing radiation aimed to replace the low sensitivity GM-counter starts after WW II. The commercial introduction of artificial radionuclides starts in 1946 following the development of cyclotron in 1930 and the nuclear reactor in 1942. $^{131}$I is the first reactor product introduced into medicine for diagnostic and treatment of thyroid gland. In-vivo distribution of $^{131}$I in thyroid gland is mapped by hand held GM-counter. The scintillation crystal NaI[Tl] with a better detection sensitivity replaces the GM-counter in 1954 and become a detector of choice in nuclear medicine instruments for the years to come. The first automated instrument to depict in-vivo distribution of $^{131}$I – rectilinear scanner is built by B.Cassen in 1955. The main limitation of this instrument is its long acquisition duration because of sequential data acquisition. On that time the direct imaging by a large area scintillation crystal is considered impossible until 1956 when Hal Anger invents his genius circuit that makes possible to define the coordinates of a interaction of a gamma photon within a scintillation crystal. This is a milestone of the epoch of nuclear medicine. The real growth in nuclear medicine dates from 1962 when $^{99m}$Tc is commercially available. Interfacing dedicated computers to gamma cameras leads to avalanche like improvement of its performance and offer the opportunity for processing of images and the generation of numerical and graphical presentation of the data. SPECT gamma cameras in the 1980’s cause the change from circular to rectangular field of view of the detector. And finally after long period of investigation and experiments PET appears in the routine clinical practice.

Key words: Anger, gamma camera
DEVELOPMENT OF A NEW TLD HOLDER FOR EYE LENS DOSIMETRY IN INTERVENTIONAL RADIOLOGY

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Abstract

This study presents the new TLD holder „XRayM“ to be used for eye lens dosimetry in interventional radiology and cardiology. Within the Project 19D/2015 of the Medical University, Sofia, a new ergonomic dosemeter with thermoluminescent detectors (TLD) was designed, produced and calibrated to be used in photon fields, for correct measurement of Hp(3). The energy response of the dosemeter was reduced in order to increase the measurement accuracy. Investigations for filter type and filter thickness were performed in the Secondary Standard Dosimetry Laboratory (SSDL), Sofia with Standard Narrow energy spectra. The new holder of dimensions 40 x 20 x 4 mm\textsuperscript{3} was constructed to contain two MCP-N (LiF:Mg,Cu,P) detectors, located under two semi-spheres, made of aluminum of 1.2 mm thickness and polymetil-metacrilat of 1 mm thickness. The energy dependence of the response of the TLD was found to be within ±(15÷25) % for PMMA and up to -20 % for Al filters. The energy compensation method was applied and the weighted response of the detectors was calculated. The results showed ± 10 % energy dependence of the new dosemeter in the energy range between 30 and 100 keV.
Introduction

The radiosensitivity of the eye lens is a well-known tissue reaction [1]. The International Commission on Radiological Protection (ICRP) Report 118 [2] determines the threshold value for acute or protracted exposures at absorbed dose to the eye lens of 0.5 Gy. Based on this, the ICRP recommended decrease of the annual eye lens dose limit for occupational exposure from 150 mSv to 20 mSv. The staff performing fluoroscopy guided interventional procedures [3], working in close proximity to patients, is shown to be at risk for exceeding the new dose limit for the eye lens. Because of the various and complex factors influencing the eye lens exposure, like distance between patient and medical staff, beam orientation, procedure complexity, skills, training and use of protective equipment during interventional procedures [4], a dedicated eye lens dosimetry is the only suitable method for correct determination of the eye lens dose in interventional radiology. The readings of the whole body dosemeters are not representative for the exposure of the eye lens due to their location: under protective clothing and far from the eyes. The dosemeter has to be worn as close as possible to the eye lens in order to reduce the inaccuracy in estimation of eye lens dose. The need to wear an extra dosemeter in addition to the mandatory whole body dosemeter should also consider clinical workload, practicality and ergonomic factors. Based on these considerations, the characteristics of an eye lens dosemeter for individual monitoring purposes should have a suitable response in recommended operational quantity, small dimensions and easy attachment to various surfaces close to the eye. If successful, the development of a convenient dosemeter with better accuracy, placed at the collar or as close as possible to the eye, will significantly improve the quality of dose measurements. Such a dosemeter would be of particular importance in situations when protective screens or eye goggles are not used.

Passive dosemeters based on thermoluminescent (TL) detectors are the usual choice because of their small size, availability and characteristics. The basic structure of a TL dosemeter includes: TL detectors, sufficient filtration and a holder to allow the dosemeter to be appropriately positioned. The holder’s shape is selected from ergonomic considerations [5]. Detector materials, filters and moderators have to be chosen to achieve flat energy response. Using materials with different densities allow modifying the energy dependence of TL detectors in the working photon energy range from 30 to 100 keV, where the most commonly used TL materials have strong energy dependence. An ideal dosemeter...
for eye lens dose assessment should have a good response for the recommended dose quantity personal dose equivalent, $H_p(3)$; the response should not vary with energy and direction of the incident radiation [6]. The dosemeter should be worn as close as possible to the eye, in contact with the skin, and facing towards the radiation source. When used in interventional radiology, the position closest to the X-ray primary beam shall be chosen [7].

**Materials and Methods**

**Preliminary tests**

MTS-N (LiF:Mg, Ti) TL detectors were used in estimating the type and thickness of the filter material. Six different filter materials were used for the tests: 1.8 mm thick polymethyl-metacrilat (PMMA), 1 mm thick aluminum (Al), 0.1 mm copper (Cu), 0.1 mm thick cadmium (Cd), 0.8 mm tin (Sn) and 0.5 mm lead (Pb).

The irradiation was performed at the SSDL, Sofia, with two types of photon beams: the narrow X-ray spectrum „N“ series described in ISO 4037 -3 standard [8], and gamma-rays of $^{137}$Cs. Water filled slab phantom with dimensions 30 x 30 x 15 cm$^3$ was used for the tests. For each radiation quality, four TLD chips were positioned behind each filter. The reading of TLDs was carried out with PCL3 Automatic TLD Reader (FIMEL). The readout parameters were chosen as follows: preheating at 150 °C, heating at constant temperature of 260°C.

„XRayM“ energy dependence

In result of the preliminary tests a new cassette named „XRayM“ with TLD holder and filters was designed and tested at the SSDL–Sofia. Five reference photon X-ray radiation qualities, specified in ISO standard 4037 and $^{137}$Cs were reproduced. Water filled cylindrical phantom, representing a head and with diameter of the central part of 20 cm, developed within the Project 23D/2014 of the Medical University, Sofia, was used. Conversion coefficients from air kerma to personal dose equivalent $H_p(3)$ were taken from Behrens et al [9]. In each exposure, two „XRayM“ and three EYE-D™ dosemeters (RADCARD) were used to verify and compare the results (Figure 1). The readings were carried out with RE-2000 TLD Reader (MIRION). The readout parameters were as follows: heating at constant temperature of 240°C, for 30s. The process of heating was carried out by nitrogen flow: 4.5 l/min. $H_p(3)$ was set to 1.0 mSv at the measurement point at 200 cm distance from the X-Ray and $^{137}$Cs sources respectively.
Figure 1. a) The X-ray set-up for energy dependence tests, b) The cylindrical phantom with "XRayM" and EYE-D™ dosemeters.

Results

Preliminary test for filter material selection

The response of the detectors behind each filter, normalized to $^{137}$Cs is presented in Figure 2. The horizontal axis refers to the radiation quality of the beam; the vertical refers to the relative detector response normalized to $^{137}$Cs.

Figure 2. The relative responses with regard to Hp(3, 0°) for 1.8 mm thick polymethyl-metacrilat (PMM, 1 mm thick aluminum (Al), 0.1 mm copper (Cu), 0.1 mm thick Cadmium (Cd), 0.8 mm tin (Sn) and 0.5 mm lead (Pb) filters as a function of the mean photon energy. The response was normalized to 137 Cs gamma radiation.
The results for the Pb, Sn, Cd filters show up to -90% underestimation of the dose in the low energy series - N40 and N60. An overestimation up to two times was found for N40 and N60 series for PMMA filter. For Cu filter, overestimation up to two times was observed for spectrums between N60 and N100, and from 30 % to 50 % for the Al filter for N40 to N100 series. Considering that the filter material has to be plastic and easily available at a reasonable price, thinner Cu and thicker Al filter were selected for further investigations.

**Preliminary test for filter thickness selection**

The aim of these tests was to further flatten the energy dependence of the TLD by proper selection of filters. Al and Cu filters of high purity (>99 %) were used. The analysis of the previous results and practical considerations led to a modified experimental set-up. Two sets of identical filters of Al and Cu were used, with TLDs placed between them, to ensure symmetry of the TLDs response in case of backside irradiation. The relative energy dependence for Al filters is presented at Figure 3a and for Cu filters in Figure 3b.

![Figure 3. a) TLD relative output with filter thickness of 1.5 mm Al, compared to 1.0 mm Al](image-url)
According to these results, the relative energy dependence of the TLDs normalized to $^{137}\text{Cs}$ was estimated to be between $-10\%$ and $+20\%$ when using 1.5 mm Al filter, while for thinner 1.0 mm Al filter the TLD relative response is between $-5\%$ and $+60\%$. When using 0.5 mm Cu filter the relative energy dependence is close to zero for N40 and up to $-20\%$ for N120. As a result of this comparison, the 1.5 mm Al filter was selected as the most appropriate for the new „XRayM“ dosemeter.

„XRayM“ construction

During the construction phase of the „XRayM“ cassette, the following requirements were considered: 1) low energy dependence in the useful energy range; 2) small dimensions and ergonomic design; 3) independency of result on which side the dosimeter is irradiated. The new cassette consists of two separate plastic parts with hemisphere filters between them, and easily fixed together by screw. The shape and dimensions of the plastic holder are presented in Figure 4.
Two hemisphere filters are implemented in the front plastic part: one PMMA of 1.0 mm thickness and one Al of 1.2 mm thickness. The Al filter thickness was chosen to be slightly thinner than the experimental one due to the practicality in the production and reduction of the price by replacing the high purity Al with cheaper and easily available Al alloy. The back part of the holder also contains an Al flat filter of 1.2 mm thickness to ensure symmetry of the response in case of backside irradiations. The final dimensions of the „XRayM“ are 40 x 20 x 4 mm$^3$.

**Relative $H_p(3)$ energy response.**

The response of the TL detectors placed behind different filters used in the new cassette „XRayM“ (1 mm PMMA; 1.2 mm Al), as a function of the mean photon energy normalized to $^{137}$Cs is presented in Figure 5.
The relative response of the TLD behind the PMMA filter is between -25 % and +15 
%. For Al filter this result is between -25 % and -5 %. For each radiation quality the ratio 
between relative responses behind PMMA and Al filters, \( N = \frac{R_{PMMA}}{R_{Al}} \), was calculated. 
Filter analysis was used and a factor for energy dependence correction was derived in order 
to obtain the energy dependence of the dosemeter response. The results are presented in 
Table 1.

**Table 1.** Empirically derived factor for energy dependence correction.

<table>
<thead>
<tr>
<th>( N = \frac{R_{PMMA}}{R_{Al}} )</th>
<th>( k )</th>
</tr>
</thead>
<tbody>
<tr>
<td>( N \geq 1.1 )</td>
<td>0.95</td>
</tr>
<tr>
<td>( N &lt; 1.1 )</td>
<td>1.25</td>
</tr>
</tbody>
</table>

The energy dependence of the new dosemeter, compared to the energy dependence 
of the commercial EYE-D\textsuperscript{TM} dosemeter is presented in Figure 6.
Figure 6. Energy response of „XRayM“; compared to EYE-D\textsuperscript{TM}.

The relative energy response of the „XRayM“ is within ± 10 %, while for the EYE-D\textsuperscript{TM} it is between -25 % and +15 %.

**Response to personal equivalent dose\( H_p(3)\).**

The response to the personal equivalent dose is determined by means of an empirical factor, related to the mean exposure energy. This correction factor will allow a reduction of the energy dependence of the TL detectors over the investigated energy range between 30 and 100 keV. According to that consideration and Table 1, \( H_p(3)\), Sv, can be calculated using the following formula:

\[
H_p(3) = k \frac{M_{PMMA}}{(R_{PMMA})_{Cs}}, \text{ Sv}
\]

Where \( H_p(3) \) is the personal equivalent dose at depth 3 mm, Sv;
\( M_{PMMA} \) is the TLD response behind PMMA filter, counts;
\( (R_{PMMA})_{Cs} \) is the sensitivity of the TLD in terms of \( H_p(3) \), according to \(^{137}\text{Cs} \), counts/Sv;
\( k \) is the empirically derived factor (Table 1).

For energies up to 65 keV, a factor of 0.95 allows to correct the over response of the detectors behind PMMA filter. For energies above 65 keV, a factor of 1.25 allows to correct
the under response of the detector. For the dosemeters used for calibration, the conditional method was applied and the results are presented in Table 2.

Table 2. The calculated personal equivalent dose \( H_p(3) \), mSv from „XRayM“, using formula presented in this work.

<table>
<thead>
<tr>
<th>( N ) series</th>
<th>( \bar{E}, \text{keV} )</th>
<th>SSDL, Sofia</th>
<th>„XRayM“</th>
<th>EYE-D\textsuperscript{TM}</th>
</tr>
</thead>
<tbody>
<tr>
<td>N 40</td>
<td>33</td>
<td>1.00 ± 0.01</td>
<td>1.09 ± 0.13</td>
<td>1.15 ± 0.08</td>
</tr>
<tr>
<td>N 60</td>
<td>42</td>
<td>1.00 ± 0.01</td>
<td>0.95 ± 0.11</td>
<td>0.97 ± 0.07</td>
</tr>
<tr>
<td>N 80</td>
<td>65</td>
<td>1.00 ± 0.01</td>
<td>1.04 ± 0.12</td>
<td>0.84 ± 0.06</td>
</tr>
<tr>
<td>N100</td>
<td>83</td>
<td>1.00 ± 0.01</td>
<td>0.99 ± 0.13</td>
<td>0.79 ± 0.06</td>
</tr>
<tr>
<td>N120</td>
<td>100</td>
<td>1.00 ± 0.01</td>
<td>0.93 ± 0.10</td>
<td>0.74 ± 0.05</td>
</tr>
</tbody>
</table>

Where \( \pm U \) is the expanded uncertainty with a coverage factor \( k=2 \), with a level of confidence 95 %. The dose response for „XRayM“ shows discrepancy from +9 % to -7 %, and for the EYE-D\textsuperscript{TM} this discrepancy is between +15 % and -26 %.

Discussion

The relative response behind filter depends on the filter material, shape and thickness, the TLD material and the radiation quality. The shape of the filters was chosen to be hemisphere to minimize the dependence of the detector response on the irradiation angulation. The filter material (Al) and the thickness of 1.5 mm were selected in result of tests with different material and thicknesses providing the best result. The thickness of 1.2 mm Al used in the final product was found to be a good compromise between Al purity, price and relative response of the dosemeter. The observed response is explained by the presence of impurities of high atomic number elements in the Al alloy used in the final product. This can be explained by the fact that in the energy range of interest the main type of photon interactions for Al are the photoelectric effect and the Compton scattering, with photoelectric effect being predominant up to 60 keV. For PMMA within the same energy range the \( Z_{eff} \) varies from 2.7 to 3.5 depending on the energy [10], therefore Compton scattering is predominant. Despite the reduced response, the presence of impurities in Al improves the production effectiveness and accuracy by reducing the risk of splitting the
The new eye lens dosemeter „XRayM“ has lower energy dependence compared to the commercially available EYE-D™. The energy dependence can be further reduced by applying a correction based on the filter analysis. The final result is reduced overall uncertainty of the measurement.

As next and final step, the angular response of the dosemeter needs to be tested. Also, because of the small size, the „XRayM“ has a potential to be used for dosimetry of the extremities, therefore the response with regard to \( H_p(0.07) \) has to be tested.

**Conclusions**

An essential aspect of quality assurance in individual monitoring is assessing the quality of the measurement result [7]. The energy dependence of the dosemeter response has a significant contribution to the uncertainty. This paper presents different phases in designing and testing of the „XRayM“ TL dosemeter to be used in interventional radiology. The new eye lens dosemeter „XRayM“ has energy dependence in the range ± 10 % that is lower compared to a commercially available similar product. An important factor for easier future utilization for routine dosimetry is the „XRayM“ four times lower price compared to the commercial product.
References:

7. ISO 15382:2015 Radiological protection, Procedures for monitoring the dose to the lens of the eye, the skin and the extremities.
Session
Biomedical Engineering
COMPARATIVE STUDY OF T-WAVE ALTERNANS IN ADULTS AND YOUNG COMPETITIVE ATHLETES

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Abstract

Alternans of T-wave (TWA) could predict arrhythmic and sudden cardiac death risk at various clinical settings. Our aim was to evaluate the presence of T-wave alternans in two different populations: young athletes performing cardiopulmonary stress test and elderly people who performed diagnostic stress electrocardiographic (ECG) test. We studied 414 young competitive athletes, and 107 elderly patients. We detected and considered continuous occurrence (packets of more than 30 s) of TWA alternans. In the athletes, there were at least one packet in 329 subjects (79.5%), while in the elderly group we observed at least one TWA packet in 10 (9.3%) patients, and this results may seem surprising. These differences can be better described considering the different test conditions of the two groups, mainly the duration and the heart rate observed during the test. It is known that the TWA occurrence depends on the hearth rate – as higher is the hearth rate (HR), as greater is the possibility for TWA. In order to obtain a more meaningful comparison, the evaluation of number of packets have been performed considering equal mean HR rate for the two populations. The range of HR in which there were TWA detection in both groups of patients was from 80 bpm to 125 bpm. The elderly group has a TWA presence higher that the same measure in athletes. In conclusion, the quantitative analysis of TWA in two different populations has permitted a comparative study of the behaviour of an arrhythmic risk factor.

Introduction

Sudden cardiac deaths (SCD) in competitive athletes is highly visible and emotional event with significant liability considerations. It is frequently subjected to intense public scrutiny because of SCD occurrence in young and otherwise healthy appearing individuals [1].

Cardio-pulmonary stress tests provides a very good information about athlete’s training level, and can reveal some presently unknown pathologies. Temporal suspension from active sports can help a lot to distinguish physiological from pathological cardiac changes in athletes, especially in cases with borderline manifestations of pathology [2-4].
Leading cardiologists supported such a strategy during a Workshop on Sports and Arrhythmias in 2009 [5], where a special chapter is dedicated on ‘Detraining is a useful tool to assess the prognostic value of ventricular arrhythmias’.

Athletes with conditions representing a high risk of SCD, should be strongly advised to stop active sports, despite the high social and economic costs of such a decision [1,6].

Alternans of T-wave (TWA) could predict malignant arrhythmia, Torsade de Pointes and sudden cardiac death risk and our research group has already performed several studies on this topic in various clinical settings: patients undergoing coronary artery bypass grafting [7-8], such with renal disease [9], diabetes mellitus [10], during diagnostic stress ECG tests [11], during diagnostic test for Brugada syndrome [12].

There is a shortage in the scientific literature of TWA studies in athletes. In a research on 85 athletes, all with ventricular arrhythmias, but without heart disease [13], they claimed that TWA is a risk stratification factor.

The aim of the current research is to evaluate and compare the presence of T-wave alternans in two different populations: young athletes performing cardiopulmonary stress test and Adults people who performed diagnostic stress electrocardiographic (ECG) test.

Material and Methods

Study group - Cardiopulmonary stress test of young competitive athletes. The cardiopulmonary stress test data was collected at Euro-Vita Sport and Dental Clinic, Sofia, Bulgaria, as part of the annual work-up of competitive athletes. The database of the current study comprises 414 young competitive athletes, 24±8 years, 395 (95.5%) males. The competitors are from the following sports: football, rhythmic gymnastics, badminton and tennis. The median duration of the exercise test was 15.27 minutes (14.8 and 16.9 respectively for the 25% and 75% percentiles), with a median heart rate of 145.6 bpm (133.3 and 156.4 percentiles).

Study group - Diagnostic stress ECG test of Adults. ECG data of 107 Adults individuals was collected at the National Cardiology Hospital, Sofia, Bulgaria. The stress test was performed using veloergometer (GE Marquette Stress PC ECG Application) – 2-min stages 25W incremental workload. The median duration of the exercise test was 7.08 minutes, and the mean heart rate was 96 bpm. The characteristics of the database are: age 63±10 years, 45 males, 39 with diabetes mellitus (DM), 85 with angina pectoris, 8 with a history of
myocardial infarction (MI), 48 with angiographically significant coronary artery disease (AS-CAD). Controllable risk factors (smoke, high blood pressure, high blood cholesterol, and obesity), not controllable risk factors (gender, age and heredity) and other clinical data are presented in Table 1. In 34 patients (32%) the stress test was positive.

Ex smokers were considered individuals who quitted from at least 6 months. The test was considered positive in the setting of ≥ 1 mm horizontal or downward-sloping ST depression 80 msec after J-point.

Signal preprocessing. Signal preprocessing was performed on all recordings to eliminate/suppress the typical noise that accompanies the ECG. The 50 Hz interference was eliminated by a removal procedure [14], the electromyographic noise was suppressed by dynamic application of an approximation procedure [15,16], and baseline drift was suppressed

Table 1. Distribution of the cardiac risk factors and clinical variables for the whole group of individuals. SD – standard deviation; BMI – body mass index; DM – diabetes mellitus; AH – arterial hypertension; MI – myocardial infarction; AS-CAD - angiographically significant coronary artery disease; PCI – percutaneous coronary intervention; n – number.

<table>
<thead>
<tr>
<th>Clinical variable</th>
<th>Distribution (n = 107)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age – mean ± SD</td>
<td>62.8 ± 10.3</td>
</tr>
<tr>
<td>Male – n (%)</td>
<td>45 (42%)</td>
</tr>
<tr>
<td>BMI – mean ± SD</td>
<td>28.0 ± 4.3</td>
</tr>
<tr>
<td>AH – n (%)</td>
<td>96 (90%)</td>
</tr>
<tr>
<td>DM – n (%)</td>
<td>39 (36%)</td>
</tr>
<tr>
<td>Dyslipidemia – n (%)</td>
<td>87 (81%)</td>
</tr>
<tr>
<td>Total cholesterol (mmol/l) – mean ± SD</td>
<td>5.09 ± 1.1</td>
</tr>
<tr>
<td>Triglycerides (mmol/l) – mean ± SD</td>
<td>2 ± 1.8</td>
</tr>
<tr>
<td>Family history of CAD – n (%)</td>
<td>11 (10%)</td>
</tr>
<tr>
<td>Smokers (present or ex) – n (%)</td>
<td>41 (39%)</td>
</tr>
<tr>
<td>Angina pectoris – n (%)</td>
<td>85 (80%)</td>
</tr>
<tr>
<td>History of MI – n (%)</td>
<td>18 (17%)</td>
</tr>
<tr>
<td>Positive stress ECG test – n (%)</td>
<td>34 (32%)</td>
</tr>
<tr>
<td>AS-CAD – n (%)</td>
<td>48 (45%)</td>
</tr>
<tr>
<td>PCI – n (%)</td>
<td>40 (37%)</td>
</tr>
<tr>
<td>Coronary artery bypass grafting – n (%)</td>
<td>10 (9%)</td>
</tr>
<tr>
<td>Stroke</td>
<td>6 (6%)</td>
</tr>
</tbody>
</table>
by a high-pass recursive filter with a cut-off frequency of 0.64 Hz [17]. Summary of all technics used for preprocessing ECG to detect TWA were described in [18].

TWA was detected by analysis of: T-wave amplitude in a combined lead and T-wave complexity obtained by the method of Principal Component Analysis (PCA). The method was described in [19], and approved in PhysioNet / Computers in Cardiology Challenge [20].

We performed the TWA identification in the entire ECG recordings, and considered the presence of "TWA packet" in case of a continuous occurrence of TWA for a minimum duration of 30 seconds.

Ethics. In order to be included in the registry, patients had to sign an informed consent for personal data analysis, and to agree to be followed up according to protocol. The study protocol is in accordance with the Declaration of Helsinki.

Statistical analysis. Statistical analyses were performed using SPSS statistical software for Windows version 20.0. The distribution of continuous variables was tested using the Kolmogorov-Smirnov test. Normally distributed data were presented as mean ± standard deviation (SD), whereas non-normally distributed data – as median and interquartile range (IQR) (the difference between the 25th and 75th percentile). Categorical variables were presented in percentage terms. We compared demographic characteristics and ECG features at rest and during exercise using independent groups test for normally distributed data and the Mann-Whitney U test for non-normally distributed data.
Results

We detected TWA alternans in all ECG recordings in the Adults and in the athletes groups, and performed the “TWA packets” identification. The median duration of the stress test and the values of HR in the two group of individuals are reported in Table 2.

Table 2. Duration of stress test and HR values in the Athlete and Adults (median values, [25th - 75th ] percentiles).

<table>
<thead>
<tr>
<th></th>
<th>Athletes (n=414)</th>
<th>Adults (n=107)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stress Test duration</td>
<td>15.3 m [14.8 – 16.3]</td>
<td>7.8 m [5.52 – 8.4]</td>
</tr>
<tr>
<td>HR</td>
<td>145.6 bpm [133.3 – 156.4]</td>
<td>94.9 bpm [86.7 – 105.0]</td>
</tr>
</tbody>
</table>

Figure 1. TWA packets during stress ECG recordings in a group of Athletes.
Figure 2. TWA packets during stress ECG recordings in Adults.

Fig. 1 reports the TWA packet identified in 100 Athletes while Fig. 2 reports the results for all the Adults (107 individuals). The two figures show predominant (and quite astonishing) presence of TWA packets in Athletes, compared to Adults.

In the athletes, there were at least one packet in 329 subjects (79.5%), while in the Adults we observed at least one TWA packet in 10 (9.3%) individuals, and this results may seem surprising. The predominance of TWA in Athletes, vs. Adults for the different number of TWA packets (from 0 to 3) is presented in Table 3.

Table 3. Number of TWA packets in Athletes and Adults.

<table>
<thead>
<tr>
<th></th>
<th>Athletes (n=414)</th>
<th>Adults (n=107)</th>
</tr>
</thead>
<tbody>
<tr>
<td>three TWA packets</td>
<td>9 (2.2%)</td>
<td>1 (0.9%)</td>
</tr>
<tr>
<td>two TWA packets</td>
<td>99 (23.9%)</td>
<td>1 (0.9%)</td>
</tr>
<tr>
<td>one TWA packet</td>
<td>221 (53.4%)</td>
<td>8 (7.5%)</td>
</tr>
<tr>
<td>no TWA packets</td>
<td>85 (20.5%)</td>
<td>97 (90.7%)</td>
</tr>
</tbody>
</table>

The surprising results of Table 3 can be explained by:

- Different test conditions. Due to fatigue, the duration of the test in Adults is interrupted long before reaching the maximal load. As seen in Table 2 the median test duration in
Athletes is almost twice longer the duration in Adults (15.3 min vs 7.8 min). This implies a greater number of TWA packets in Athletes than in Adults.

- Different functional conditions. It is known that the TWA occurrence depends on the hearth rate – as higher is the hearth rate, as greater is the possibility for TWA. Due to premature interruption of the test (caused by fatigue) and due to the slower load-dependant rise of the heart rate in adults, the median HR in Athletes is much greater than in Adults (145.6 vs. 94.9 bpm, as seen in Table 2). The slower load-dependant rise of HR in Athletes vs. Adults is shown in Figure 3.

The TWA characteristics of the two study groups as: TWA total durations, TWA median and maximal amplitude, HR-dependant appearance of the 1st and 2nd TWA packets, are presented in Table 4.

![Figure 3. Load-dependent HR rise of two individuals from Athletes (blue) and Adults (red).](image-url)
Table 4. TWA characteristics in Athletes and Adults. (Median values, [25th - 75th ] percentiles).

<table>
<thead>
<tr>
<th></th>
<th>Athletes (n=414)</th>
<th>Adults (n=107)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total TWA duration</td>
<td>3.94 m [2.2 – 5.8]</td>
<td>1.43 m [0.87 – 2.74]</td>
</tr>
<tr>
<td>TWA duration percentage</td>
<td>25.7 % [15.1 – 37.6]</td>
<td>16.45 % [9.0 – 27.4]</td>
</tr>
<tr>
<td>TWA mean amplitude</td>
<td>0.41 µV [0.23 – 0.90]</td>
<td>0.40 µV [0.13 – 0.72 ]</td>
</tr>
<tr>
<td>TWA max amplitude</td>
<td>0.92 µV [0.50 – 1.92]</td>
<td>0.84 µV [0.29 – 1.21]</td>
</tr>
<tr>
<td>Mean HR in the test</td>
<td>146 bpm [133 – 156]</td>
<td>95 bpm [87 – 105]</td>
</tr>
<tr>
<td>Mean HR in 2nd packet</td>
<td>143 bpm[124 – 170]</td>
<td></td>
</tr>
</tbody>
</table>

In order to obtain a more meaningful comparison, the evaluation of number of packets have been performed considering equal mean HR rate for the two populations. The range of HR in which there were TWA detection in both groups of individuals was from 80 bpm to 125 bpm.

Figure 4 reports the HR distribution of the number of TWA packets in Athletes and Adults, and the red lines delimit the region of interest.

Table 5 reports the range 50-230 bpm which is divided in 12 intervals, where the 2nd and 4th columns report the number of individuals with a mean HR (considering the 60 beats of the TWA window) in the corresponding HR interval range, while 3rd and 5th columns report...
the corresponding number of individuals with a TWA packet in the same range. Also in this case, red characters underline the rows of interest.

Table 5. Presence of TWA packets in the Adults and Athletes groups, at different HR ranges

<table>
<thead>
<tr>
<th>HR range bpm</th>
<th>Adults</th>
<th></th>
<th>Athletes</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Total N (%)</td>
<td>with a TWA packet n (%)</td>
<td>Total N (%)</td>
<td>with a TWA packet n (%)</td>
</tr>
<tr>
<td>50-65</td>
<td>5 (4.7%)</td>
<td>0 (0.0%)</td>
<td>29 (7.0%)</td>
<td>0 (0.0%)</td>
</tr>
<tr>
<td>65-80</td>
<td>67 (62.6%)</td>
<td>0 (0.0%)</td>
<td>132 (31.9%)</td>
<td>0 (0.0%)</td>
</tr>
<tr>
<td>80-95</td>
<td>100 (93.5%)</td>
<td>1 (1.0%)</td>
<td>295 (71.3%)</td>
<td>6 (2.0%)</td>
</tr>
<tr>
<td>95-110</td>
<td>89 (83.2%)</td>
<td>3 (3.4%)</td>
<td>392 (94.7%)</td>
<td>6 (1.5%)</td>
</tr>
<tr>
<td>110-125</td>
<td>61 (57.0%)</td>
<td>6 (9.8%)</td>
<td>411 (99.3%)</td>
<td>21 (5.1%)</td>
</tr>
<tr>
<td>125-140</td>
<td>30 (28.0%)</td>
<td>0 (0.0%)</td>
<td>411 (99.3%)</td>
<td>42 (10.2%)</td>
</tr>
<tr>
<td>140-155</td>
<td>8 (7.5%)</td>
<td>0 (0.0%)</td>
<td>408 (98.6%)</td>
<td>51 (12.5%)</td>
</tr>
<tr>
<td>155-170</td>
<td>5 (4.7%)</td>
<td>0 (0.0%)</td>
<td>387 (93.5%)</td>
<td>101 (26.1%)</td>
</tr>
<tr>
<td>170-185</td>
<td>0 (0.0%)</td>
<td>0 (0.0%)</td>
<td>344 (83.1%)</td>
<td>84 (24.4%)</td>
</tr>
<tr>
<td>185-200</td>
<td>0 (0.0%)</td>
<td>0 (0.0%)</td>
<td>226 (54.6%)</td>
<td>17 (7.5%)</td>
</tr>
<tr>
<td>200-215</td>
<td>0 (0.0%)</td>
<td>0 (0.0%)</td>
<td>44 (10.6%)</td>
<td>0 (0.0%)</td>
</tr>
<tr>
<td>215-230</td>
<td>0 (0.0%)</td>
<td>0 (0.0%)</td>
<td>1 (0.2%)</td>
<td>0 (0.0%)</td>
</tr>
</tbody>
</table>

Considering the range of interest, the Adults has an occurrence of TWA packets higher that the same measure in Athletes. For example the presence of TWA of the Athlete group were 2.0%, 1.5% and 5.1% of cases in the HR range [80-95bpm], [95-110bpm], and [110-125bpm] respectively; while the TWA in Adults were 1.0%, 3.4% and 9.8% in the same HR intervals.

Table 6 shows some characteristic of TWA packets considering only patients with TWA packets in the range 80-125 bpm. From this Table, it turns out that Athletes have lower TWA packets with max and mean TWA amplitudes than Adults.

Discussion

The detection of TWA packages showed a surprising apparently prevalence of TWA in Athletes than in the group of Adults (at least one packet of more than 30 sec in 329 Athletes (79.5%), vs. 10 (9.3%) in Adults). Besides part of the Adults contingent had registered various heart diseases or other diseases worsening the cardiac function (Table 1), such as: diabetes mellitus, arterial hypertension, myocardial infarction, angiographically significant coronary artery disease, percutaneous coronary intervention, etc. TWA parameters in Athletes were...
worse than those in Adults (Table 4): TWA mean amplitude 0.41 µV in Athletes vs. 0.40 µV in Adults and TWA max amplitude 0.92 µV in Athletes vs. 0.84 µV in Adults.

Nevertheless, the two groups are studied in different Test conditions. In fact, considering that the TWA manifestation depends on the HR, we concentrate the comparison to the common HR ranges of the two study groups.

The reduced comparison changed radically the results and this can be seen in Table 5 (text in red colour). For example, TWA is presented in 9.8% and 3.4% of the adults and 5.1% and 1.5% in Athletes for a HR of 110-125 and 95-110 bpm respectively. This is seen also in Figure 4 where the 80-125 bpm range is marked by 2 vertical red lines.

The appropriate reduced comparison changed also the TWA characteristics in favour of Athletes and this can be seen in Table 6.

### Table 6. TWA characteristics in Athletes and Adults considering TWA packets in the range 80:125. (Median values, [25th - 75th] percentiles).

<table>
<thead>
<tr>
<th></th>
<th>Athletes (n=33)</th>
<th>Adults (n=10)</th>
</tr>
</thead>
<tbody>
<tr>
<td>TWA mean amplitude</td>
<td>0.34 µV [0.12 – 1.47]</td>
<td>0.40 µV [0.13 - 0.72]</td>
</tr>
<tr>
<td>TWA max amplitude</td>
<td>0.72 µV [0.24 – 2.93]</td>
<td>0.84 µV [0.29 - 1.21]</td>
</tr>
<tr>
<td>Mean HR in the test</td>
<td>127 bpm [115 – 144]</td>
<td>103 bpm [101 – 110]</td>
</tr>
<tr>
<td>Mean HR in 1st packet</td>
<td>111 bpm [101 – 120]</td>
<td>115 bpm [107 – 116]</td>
</tr>
<tr>
<td>Mean HR in 2nd packet</td>
<td>152 bpm [125 – 159]</td>
<td>-</td>
</tr>
</tbody>
</table>

### Conclusion

T-wave alternans detection was performed on ECGs, recorded during cardiopulmonary test of young competitive Athletes. The study showed a significant presence of TWA packets of 30 and more seconds. Packets of TWA were detected also in ECGs of Adults, recorded during stress test. The HR range-dependent comparison showed predominant amount of TWA in Adults. The alternans characteristics were also in Athletes’ favour. Despite the positive result of the comparison, the detected amount and duration of TWA in Athletes are relevant and require additional study.

### Acknowledgments

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References


ULTRASOUND IMAGING: SIGNAL ACQUISITION, NEW ADVANCED PROCESSING FOR BIOMEDICAL AND INDUSTRIAL APPLICATIONS

J. Przondziono¹, W. Walke², J. Szala¹, J. Wieczorek¹

¹Silesian University of Technology, Katowice, Poland; ²Silesian University of Technology, Gliwice, Poland

Use of ultrasound, namely in the biomedical diagnosis and industrial fields, pioneered in 1950s, is today particularly widespread. In the last decades, ultrasound imaging has benefited from advances in numerical technologies such as signal processing. On the other hand, the use of ultrasound imaging has increased the need for signal processing techniques. This paper presents a review and the up-to-date developments in ultrasound imaging techniques, including elementary principles, signal acquisition and processing, from one dimensional to multidimensional systems. This paper also deals with typical relevant applications.

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There is a problem connected with application of steel guide wire, namely creation of microthrombi on their surface. It is caused by haemostatic activity of metallic materials. Therefore, proper modification of wire surface after drawing is essential. The purpose of this study is to analyse changes of structure and geometrical features of the surface of wires made of stainless steel X10CrNi18-8 after drawing and after further steps of surface modification. The surface of drawn wire was subject to mechanical grinding, electrochemical polishing and chemical passivation, consecutively. Such treatment is aimed at increasing wire resistance to electrochemical corrosion.

There is a problem connected with application of steel guide wire, namely creation of microthrombi on their surface. It is caused by haemostatic activity of metallic materials. Therefore, proper modification of wire surface after drawing is essential.

- **Key words:** acoustic signal detection; biomedical ultrasonics; medical image processing; multidimensional signal processing
COMPLEX ANALYSIS OF ASYMPTOMATIC CAROTID STENOSIS AND RESTENOSIS-ACCORDING PARAMETERS- ABI, FMD AND IMT OF HUMAN CAROTID ARTERIES-RESTENOSIS AS A CONSEQUENCE OF THE LOCAL STRAIN STRESS

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\(^2\)Department of Neurology; Faculty of Medicine; Medical University-Sofia, Sofia, Bulgaria
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Abstract

Impaired endothelial function and increased carotid intima-media thickness are key events in the atherosclerotic process and predict future cardiovascular events in subjects with and without coronary artery disease. The purpose of this study was to investigate whether the vasodilator response to increased flow in the brachial artery and the presence of carotid lesions may have a prognostic significance for in-stent restenosis in patients undergoing carotid angioplasty.

Arterial endothelial dysfunction is one of the key early events in atherogenesis, preceding structural atherosclerotic changes. It is also important in the late stages of obstructive atherosclerosis, predisposing to constriction and/or thrombosis.

The study population included 32 patients with carotid artery stenosis, 5 healthy volunteers, and 18 with restenosis within 6 years after stenting. All patients underwent ultrasound detection of brachial artery reactivity. Flow mediated dilatation (FMD) was investigated after 5 minutes of occlusion of the artery and nitroglycerin mediated dilation (NMD).

Working hypothesis is influence of the power of action of the stent over carotid arterial wall, as a main reason for depositing of alpha fibrils and prompt restenosis within few years.

Key words: endothelial function, flow-mediated dilatation, ultrasound, Ankle brachial pressure index-ABI, Intima media thickness-IMT
Introduction

Endothelial function can be measured in corotide arteries and in the periphery according to Campuzano R., et al. 2003, by measuring vasomotor function after intra-arterial infusion of pharmacologic substances which enhance the release of endothelial nitric oxide and with combination with Doppler ultrasound (Hitachi, Aloka-Alpha-6; Japan). Advantage of these methods is their non-invasive nature, which generally makes them suitable for studies involving asymptomatic subjects. For this reason, noninvasive tests of endothelial function have been developed. In the most widely used of these, an ultrasound-based method, arterial diameter is measured in response to an increase in shear stress, which causes endothelium-dependent dilatation (flow mediated dilation-FMD) (Pyke K.E. and Tschakovsky M.E., 2005). Endothelial function assessed by this method correlates with invasive testing of coronary endothelial function, as well as with the severity and extent of corotide atherosclerosis and stenosis.

Ankle brachial index -ABI is a noninvasive vascular screening test to identify large vessel peripheral arterial disease by comparing systolic blood pressures in the ankle to the higher of the brachial systolic blood pressures, which is the best estimate of central systolic blood pressure (Allison M.A. et al., 2008; McDermott M.M. et al., 2000).

Intima media thickness (IMT) of large artery walls, especially carotid, can be assessed by B-Mode ultrasound in a relatively simple way and represents a safe, inexpensive, precise and reproducible measure. IMT is used to detect the presence of atherosclerotic disease in humans and, more contentiously, to track the regression, arrest or progression of atherosclerosis. Ultrasound IMT measurements have been first proposed and in vitro validated in Milan by Paolo Pignoli in 1984 and later publicized in a most cited article. The use of IMT as a non-invasive tool to track changes in arterial walls has increased substantially since the mid-1990s. Although IMT is predictive of future cardiovascular events

This noninvasive endothelial function testing has provided valuable insights into early atherogenesis, as well as into the potential reversibility of endothelial dysfunction by various strategies, including pharmacological agents (lipid lowering, ACE inhibition), L-arginine, nicardipine, antioxidants and hormones.

Vascular echography was performed to measure intima media thickness (IMT) of carotid arteries. At baseline we evaluated all the established traditional cardiovascular risk factors. We also subdivided our study cohort according to values of FMD in patients with FMD above and patients below the median value.

Evaluation of ABI, FMD and carotid IMT may provide important prognostic information in patients with stenosis in order to prevent restenosis with regulation of power of action of the stent on vascular wall.
Assessment of Ankle brachial index - ABI by means Doppler ultrasound

This noninvasive endothelial function testing has provided valuable insights into early atherogenesis, as well as into the potential reversibility of endothelial dysfunction by various strategies, including pharmacological agents (lipid lowering, ACE inhibition), L-arginine, nicardipine, antioxidants and hormones.

\[
ABPI_{\text{Leg}} = \frac{P_{\text{Leg}}}{P_{\text{Arm}}}
\]

Assessment of Flow mediated dilatation - FMD by means Doppler ultrasound

The FMD analysis can continually record and plot the whole processes from baseline through occlusion and vasodilatation to recovery, assuring that the true vasodilatation peak will never escape detection. Percent FMD another parameters are automatically and immediately calculated after the recording is complete.

The vascular endothelium is exposed to a hemodynamic stress generated by the blood flow known as the wall strain stress. Wall strain stress is defined as the force per unit area exerted on the vessel wall by the blood flow and it depends on blood viscosity and the blood flow velocity profile. The value of the wall shear stress is expressed in N/mm² and the physiologic values in the venous system range from 1 to 6 x10⁻⁷ N/mm², while in the arteries they are at least 10 to 15 x10⁻⁷ N/mm².

FMD (flow-mediated dilation), a non-invasive measure of conduit artery endothelial function

Materials and Methods

Methods-Aloka doppler ultrasound work as well: By Broadband harmonics uses the broadband and large amplitude transmission typically represented by compound impulse waveform transmission. The technique of removing the fundamental wave components by phase modulation is used. Compared with phase-modulated harmonics (based on differences
between two frequencies elsewhere used), the broadband harmonics assure a high and wide frequency distribution and generates images with straightforward sounds.

Figure 2. Experimental protocol

The study population included 32 patients undergoing percutaneous carotid artery intervention (CAI) with stenting and at least 24 months of follow-up. 5 Healthy volunteers as a control for IMT, ABI and FMD. All CAI patients are with premedication of statins and their HDL-cholesterol level is between 5.8-5.85. All patients underwent ultrasound detection of carotid artery reactivity 30 days after CAI. Flow mediated dilatation (FMD) was investigated after 5 minutes of occlusion of the artery. Vascular echography was performed to measure intima media thickness (IMT) of carotid arteries. At baseline we evaluated all the established traditional cardiovascular risk factors. We also subdivided our study cohort according to values of FMD in patients with FMD above and patients below the median value.

Database and medical records of all 32 patients included into the survey for the period 2009 to 2015.

Results

Patients with FMD above the median value showed higher prevalence of hypertension (P=0.002), diabetes (P=0.02) and carotid IMT (P=0.006) than those below the median. Brachial FMD was inversely correlated (P=0.001) to carotid IMT. At the end of follow-up clinical events occurred in nine patients. In a multivariate analysis, including all the variables evaluated at baseline, carotid IMT (P=0.02), level of glycemia (P=0.001), a lower FMD (P=0.005) and presence of carotid plaque remained the only variables predictive of restenosis.
Figure 3. Structure and function of endothelial layer and basal lamina of the blood vessel

On the left, the gate tracking in 2D is shown with the optimal visualization of tracking in M-mode; below, three carotid waves are shown; On the right (top), the selected carotid waves are shown; below the carotid wave, resulting from the analysis of at least 5 selected waves is shown with a normal value of stiffness parameters.

Figure 4. Normal values of intima media thickness, blood flow, blood pressure and heart rate

Discussion

Impaired endothelial function and increased carotid intima-media thickness are key events in the atherosclerotic process and predict future cardiovascular events in subjects with and without coronary artery disease. The purpose of this study was to investigate whether the vasodilator response to increased flow in the brachial artery and the presence of carotid lesions may have a prognostic significance for in-stent restenosis in patients undergoing corotid angioplasty.
Intima media thickness (IMT) of large artery walls, especially carotid, can be assessed by B-Mode ultrasound in a relatively simple way and represents a safe, inexpensive, precise and reproducible measure. IMT is used to detect the presence of atherosclerotic disease in humans and, more contentiously, to track the regression, arrest or progression of atherosclerosis.

Although carotid intima-media thickness is strongly associated with atherosclerosis, thickening of the intima-media may not be due to atherosclerosis. Intimal thickening is a complex process, depending on a variety of factors, including local hemodynamics, shear stress and blood pressure. Changes in shear stress may adversely affect endothelial function and particle residence time, affecting the delivery and transport of potentially atherogenic particles into the arterial wall and consequent plaque formation. Blood pressure may affect IMT through blood vessel remodeling or wall hypertrophy in response to altered circumferential stress.

Conclusions

In perspective the greater advantages concerning stenosis are:

1) To define the evolution of carotid vascular stenosis in patients with risk factors.
2) To define the burden of risk factors in vascular stiffness parameters.
3) To identify the modification of stiffness parameters very early, before the appearance of morphological alteration such IMT.
4) To evaluate, by means of follow-up the effects of medical therapy (such as HMGCoA-reductase inhibitor).
5) To study some pathophysiological mechanisms, which until today was only possible in a highly specialized laboratory.
6) To be an easy technique without being time consuming.
In perspective the greater advantages concerning re-stenosis are:
1) To estimate relationship between ABI and FMD
2) To evaluate pathophysiological mechanisms of restenosis possible due to power of action of the stent over vascular wall.

References:


NATIONAL DATABASE FOR PATIENT DOSE REGISTRATION AND ANALYSIS IN DIAGNOSTIC RADIOLOGY

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Abstract

A new MS Access software database was developed in order to facilitate the Third National Patient Dose Survey in diagnostic radiology in Bulgaria. It is inspired by an earlier database elaborated for the purposes of the First Bulgarian National Patient Dose Survey performed in frame of Bulgaria-Germany EC Phare program Twinning project (2002-2004). The database contains information for different X-ray systems and procedures included in the survey. A set of tables, queries and reports are created to facilitate the calculation of main mathematical properties for examinations included in the survey.

Results are presented for min, max, average, median, etc. values for patient anthropomorphic data and X-ray exposure parameters. Typical doses for each room and projection are derived.

Analysis of data collected from the survey up to the moment is presented and discussed.

Conclusions are drawn regarding applicability of the presented system in the process of establishing of updated National Diagnostic Reference Levels (DRLs) as a main outcome of the Third National Patient Dose Survey.

Key words: Software; Database; Data Analysis; Patient Dose; Typical Dose; National Survey, DRLs, NRRLs, Diagnostic Radiology Examinations, Exposure parameters

1 Presenting author: i.tsanev@ncrpr.org
Introduction

For the purposes of the Third National Survey of radiation exposure to patients at medical diagnostic X-ray examinations on the territory of Bulgaria (TNS), a National Database for patient dose registration and analysis in diagnostic radiology called shortly below National Database, was designed. The database was inspired to some extent by an earlier version of a patient dose database elaborated under Twinning project Bulgaria-Germany on Microsoft Access platform [1, 2]. When creating the database in the process of storing and processing of acquired information methods of collecting data within TNS were taken into account. The world practices for the presentation of results of similar studies were considered also [3-7].

Materials and Methods

The methodology for collecting data defines standardized forms in tabular format to be completed by the medical professionals performing diagnostic radiology examinations of patient. The forms and instructions for their completion are published on the website of the NCRRP at: http://www.ncrrp.org/new/en/DRL2016-c437 [8]. Completed forms are received in Section of Radiation Protection at Medical Exposure (SPRME) at the National Centre of Radiobiology and Radiation Protection (NCRRP). The information requested from medical institutions for the purposes of the TNS contains data about:

Medical establishment:
- name and location of the hospital;
- name, position and contact details of the staff member who provided the requested information;

X-ray equipment used in actual medical examination:
- type of equipment and its technological and operating characteristics;

Main exposure and dosimetric parameters:
- main anthropomorphic data of the patient;
- type and projection (if applicable) of medical examination being registered;
- basic exposure parameters of the respected examination;
- values of physical quantities displayed at the X-ray system;
A main objective of the National Survey is to derive and set National Diagnostic Reference Levels (NDRLs) for different X-ray medical examinations. Therefore, the database is structured in the form of tables allowing differentiation of data by:

- Medical institution (Hospital, Centre, Ambulance, Specialized Laboratory, etc.);
- Type of X-ray diagnostic system;
- Type of X-ray diagnostic examination;

To preserve the relationship of data corresponding relations are created:

- between data table for medical institutions and data table with the performance of specific equipment.
- between data table for the performance of the X-ray diagnostic system and data table containing data for exposure and dosimetric parameters for certain medical examination.

Due to the specifics of calculation of Average Glandular Dose (AGD) at mammography examinations, special database modules written on Visual Basic for Applications (VBA) [9] are developed for calculating conversion factors from Incident Air Kerma to AGD. These factors depend on anthropomorphic data of the individual patient and performance of mammography system. The conversion factors are calculated from their table values, published in European guidelines for quality assurance in breast cancer screening and diagnosis Fourth Edition [10, 11], using linear approximation.

![Figure 1 Examination – Roentgenography](image-url)
<table>
<thead>
<tr>
<th>Medical establishment</th>
<th>Equipment used in actual medical examination</th>
<th>Values of operating and dosimetry parameters</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Figure 2 Examinations – Fluoroscopy</strong></td>
<td><img src="image" alt="Fluoroscopy Equipment Description" /></td>
<td><img src="image" alt="Fluoroscopy Dosimetry Parameters" /></td>
</tr>
<tr>
<td><strong>Figure 3 Examinations – Angiography</strong></td>
<td><img src="image" alt="Angiography Equipment Description" /></td>
<td><img src="image" alt="Angiography Dosimetry Parameters" /></td>
</tr>
<tr>
<td>Medical establishment</td>
<td>Equipment used in actual medical examination</td>
<td>Values of operating and dosimetry parameters</td>
</tr>
<tr>
<td>-----------------------</td>
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<td>--------------------------------------------</td>
</tr>
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<td>Лечебно заведение</td>
<td>Уреди Томограф</td>
<td>Пациенти Томограф</td>
</tr>
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<td>Лечебно заведение</td>
<td>ID</td>
</tr>
<tr>
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<td>Уреда</td>
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<td>Кабинет</td>
<td>Анатомична област</td>
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<tr>
<td>тел за контакт</td>
<td>Производител</td>
<td>Брои сердни</td>
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<td>Model</td>
<td>Телесна маса</td>
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<td>Брой детекторни рядове</td>
<td>Ръст</td>
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<td>Автоматична модулация на така</td>
<td>Възраст години</td>
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<td>Влияние на дисплей</td>
<td>Възраст месец</td>
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<td>eff mA</td>
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<tr>
<td></td>
<td></td>
<td>Време на ротация</td>
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<td>Сърца на скиемане</td>
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<td>Широчина на скиемане</td>
</tr>
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<td>Режим на скиемане</td>
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<td>Протокол на измерване</td>
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<td>Coment</td>
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<td></td>
<td></td>
<td>Sum DLP</td>
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</tbody>
</table>

Figure 4 Examinations - Computer Tomography

<table>
<thead>
<tr>
<th>Medical establishment</th>
<th>Equipment used in actual medical examination</th>
<th>Values of operating and dosimetry parameters</th>
</tr>
</thead>
<tbody>
<tr>
<td>Лечебно заведение</td>
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<td>Пациенти Мамография</td>
</tr>
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<td>ID</td>
<td>Лечебно заведение</td>
<td>ID</td>
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<td>Отделение</td>
<td>Уреда</td>
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<td>Кабинет</td>
<td>Анатомична област</td>
</tr>
<tr>
<td>тел за контакт</td>
<td>Производител</td>
<td>Брои графи за пациента</td>
</tr>
<tr>
<td></td>
<td>Model</td>
<td>Гъ̀дя</td>
</tr>
<tr>
<td></td>
<td>Брой детекторни рядове</td>
<td>Процедура</td>
</tr>
<tr>
<td></td>
<td>Автоматична модулация на така</td>
<td>Дебелина на компрессираната гъ̀да</td>
</tr>
<tr>
<td></td>
<td>Влияние на дисплей</td>
<td>мишен/фильтър</td>
</tr>
<tr>
<td></td>
<td></td>
<td>kv</td>
</tr>
<tr>
<td></td>
<td></td>
<td>mAs</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Разстояние фокус-градна опора</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Коментар</td>
</tr>
<tr>
<td></td>
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<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Figure 5 Examinations – Mammography
To find analytical solutions to problems raised in TNS, SQL queries that join the tables related to specific medical examinations using the relationships between the tables are defined in the database. Queries include calculated fields for categorization of patients: age and body weight and define unique human-readable identifiers for medical equipment. Standard SQL group functions and additional custom functions developed on VBA code are used for statistical analysis of data.

-- Added Calculated Fields into Join Queries

If ([Age Years] < 15,
    If ([Age Years] < 1 and [Age Months] = 1,"Newborns",
    If ([Age Years] < 1, "Kids (0-1 y.)",
    If ([Age Years] < 5, "Kids (1-5 y.)",
    If ([Age Years] < 10, "Kids (5-10 y.)",
        "Kids (10-15 y.)"))), "Adults")

AS [Age Group]

If ([Age Group] = "Adults",
    If ([Body Weight] < 50 Or [Body Weight] > 90," abnormal", “norm”), "kid")

AS [Filter weight]

[Medical Establishment].[City] & "–" & [Medical Establishment].[Name] & “– Examination–" & [Equipment].[Maker] & "–" & [Equipment].[Room]

AS [Unicode Equipment]

--From Join Queries: Roentgenography, Fluoroscopy, Angiography and Computer Tomography

GROUP BY

[Age Group]
[Filter weight] and/or other relevant fields
[Unicode Equipment]
[Anatomic Area Imaging]

-- Group functions: Count, Minimum, Maximum, Medina, Average and Standard Deviation

-- For Fields: [Body Weight], [Stature], [DAP] etc.
In particular, additional calculated fields are included in the joined data queries for determining conversion factors necessary for the calculation of the (AGD) from Entrance Surface Air Kerma.

-- Added Calculated Fields into Join Query Mammography

$$IIf ([ Thickness \ of \ the \ compressed \ breast ] > 110, '', g_{\ TrendHVL} ([ Thickness \ of \ the \ compressed \ breast ], [ HVL_{\ Equipment} ]))$$

AS [g-conversion factor].

$$IIf ([ Thickness \ of \ the \ compressed \ breast ] > 110, '',
   IIf ([ Age ] < 50, c_{1}TrendHVL ([ Thickness \ of \ the \ compressed \ breast ], [ HVL_{\ Equipment} ]),
   IIf ([ Age ] >= 50, c_{2}TrendHVL ([ Thickness \ of \ the \ compressed \ breast ], [ HVL_{\ Equipment} ]),
   ' '')))$$

AS [c-conversion factor].

$$IIf ([ Patients \ Mammography ] \neq [ Anode / Filter ] = " Mo/Mo", 1,
   IIf ([ Patients \ Mammography ] \neq [ Anode / Filter ] = " Mo/Rh", 1.017,
   IIf ([ Patients \ Mammography ] \neq [ Anode / Filter ] = " Rh/Rh", 1.061, 1.042)))$$

AS [s-conversion factor]

$mAs \times [ Beam \ flow \ of \ 1m (\mu Gy/mAs)] \times [g-conversion \ factor] \times [c-conversion \ factor] \times [s-conversion \ factor]$ $\times [(Distance \ focus \ on \ breast \ mainstay \ (mm))^{2} - (Thickness \ of \ the \ compressed \ breast \ (mm))]^{2}$

AS [Average Glandular Dose] (Gy)

-- From Join Query: Mammography

GROUP BY

[Unicode Equipment],
[Breast Projection],
[Laterality],
[Anode / Filter];

-- Group functions: Count, Minimum, Maximum, Medina, Average and Standard Deviation

-- For Fields: [Thickness of the compressed breast], [Average Glandular Dose], etc.
Results

For verification of calculated results provided by the database, a representative subset of records (669 patients, 28 X-ray system, Chest PA radiography projection) were compared with those obtained by alternative and traceable method (MS Excel) [12]. The comparison of results obtained shows full compliance between both calculation methods.

Table 1 Comparison of calculated results obtained by MS Excel and the National Database.

<table>
<thead>
<tr>
<th>Examination Roentgenography Chest PA</th>
<th>Microsoft Excel</th>
<th>Database</th>
</tr>
</thead>
<tbody>
<tr>
<td>X-Ray System</td>
<td>Patients [count]</td>
<td>Average DAP [µGy.m²]</td>
</tr>
<tr>
<td>№</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>TUR, DRX124</td>
<td>19</td>
</tr>
<tr>
<td>2</td>
<td>Shimadzu, Flex vision HB</td>
<td>37</td>
</tr>
<tr>
<td>3</td>
<td>QMI, QC - 550</td>
<td>20</td>
</tr>
<tr>
<td>4</td>
<td>GE, Precision RXi</td>
<td>31</td>
</tr>
<tr>
<td>5</td>
<td>Siemens. Axiom Icons R200</td>
<td>14</td>
</tr>
<tr>
<td>6</td>
<td>DR</td>
<td>20</td>
</tr>
<tr>
<td>7</td>
<td>QMI, Q - Rad</td>
<td>20</td>
</tr>
<tr>
<td>8</td>
<td>Toshiba, Quantum QG 50 G</td>
<td>9</td>
</tr>
<tr>
<td>9</td>
<td>Siemens, Axiom Aristos</td>
<td>18</td>
</tr>
<tr>
<td>10</td>
<td>TUR, D 800 - 1</td>
<td>20</td>
</tr>
<tr>
<td>11</td>
<td>Siemens, Multix</td>
<td>130</td>
</tr>
<tr>
<td>12</td>
<td>Philips, Compact Diagnost</td>
<td>13</td>
</tr>
<tr>
<td>13</td>
<td>Siemens, Multix U</td>
<td>20</td>
</tr>
<tr>
<td>14</td>
<td>Siemens, Sire graph CPH</td>
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<tr>
<td>15</td>
<td>BMI, BRT 20</td>
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<tr>
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<td>Philips, Diagnost 93</td>
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<td>SITEC, DigiRad Q</td>
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<td>18</td>
<td>Siemens, Polidoros 50S</td>
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<td>19</td>
<td>Sedecal, LX Plus</td>
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<tr>
<td>20</td>
<td>Philips, Diagnost 1</td>
<td>20</td>
</tr>
<tr>
<td>21</td>
<td>ItalRay, STATIX BS45</td>
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<td>22</td>
<td>Siemens, Polimat 50</td>
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<td>Siemens, Luminous Fusion</td>
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<td>24</td>
<td>GE, Proteus XR/a</td>
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<td>EDR 750 B</td>
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<tr>
<td>26</td>
<td>Philips, Bucky Diagnost</td>
<td>19</td>
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<tr>
<td>27</td>
<td>Siemens, Polymath 70</td>
<td>19</td>
</tr>
<tr>
<td>28</td>
<td>Philips, Diagnost 1</td>
<td>20</td>
</tr>
</tbody>
</table>
Discussion

The developed National Database allows storage and processing of data of TNS at its present stage, but it does not provide automatic graphical display of the final results. The available resources in MS Access are not satisfactory for this purpose according to opinion of the authors of this work. Therefore a proper representation of statistical analysis results in a comprehensive graphical and table format is foreseen by development of dedicated procedures on specialized graphical software application, such as Microsoft Power Business Intelligence for example [13].

Conclusions

The elaborated National Database for patient dose registration and analysis in diagnostic radiology is valuable tool for storing, processing and statistics analysis of data collected during TNS. It proved to be useful for elaboration of Preliminary NDRLs for Bulgaria [14].

Acknowledgement

The authors wish to express their gratitude to Mr. Gari Kasparyan (former staff member of SRPME) and Mr. Filip Simeonov (PhD student at NCRRP) for the valuable discussions related to the subject of this work.

References:


DETECTION OF ENDOTHELIAL DYSFUNCTION USING SKIN TEMPERATURE OSCILLATIONS ANALYSIS

S. Podtaev¹, N. Zubareva², A. Parshakov², E. Smirnova²

¹Institute of Continuous Media Mechanics, Perm, Russia; ²Perm State Medical University, Perm, Russia

Objective: The purpose of this study was to examine correlations between laboratory markers of endothelial dysfunction (ED) and the degree of endothelium dependent vasodilation using wavelet analysis of skin temperature (WAST) during a local heating test in patients with peripheral arterial disease (PAD).

Materials and methods: The study population consisted of 17 healthy subjects and 38 patients with PAD and chronic limb ischemia (CLI) at stage II (12 patients), III (8 patients) and IV (18 patients). The skin temperature (ST) on the plantar surface of the first toe was measured during the test, and the inverse wavelet transform was applied to reconstruct the ST oscillations in three frequency bands corresponding to myogenic (0.052–0.145 Hz), neurogenic (0.021–0.052 Hz), and endothelial (0.0095–0.021 Hz) mechanisms of vascular tone regulation. The patency of the major blood vessels of the lower extremities was estimated based on the results of Ro-contrast agent aortic arteriography. Doppler ultrasound was performed to allow estimations of the type of blood circulation, the state of the vascular walls, the existence of atherosclerotic plaques, the value of the regional blood pressure, and the ankle–brachial index.

Results: In the healthy subjects, a local increase in temperature up to 42°C caused a >threefold increase in the amplitudes of foot ST oscillations. Among the patients with PAD, the response to the test was much weaker in all frequency ranges, which suggests the presence of dysfunction in the myogenic, neurogenic, and endothelial regulation mechanisms. Vasodilation indices (relative changes in temperature oscillations during local heating) in the endothelial range are well correlated with the laboratory markers of ED: endothelin, homocysteine, and vWF. Increased vWF levels in PAD patients indicate arterial endothelial cell damage by atherosclerotic and revascularization processes. The level of vasodilation dysfunction, described by vasodilation indices, correlated with the level of artery stenosis in the lower extremities and with the progression of CLI.

Conclusion: WAST can be considered as a low cost, portable, and easy to use technique for the noninvasive assessment of ED.

The work was supported by the Russian Foundation for Basic Research under project R-Ural-a 14-04-96027

- Key words: endothelial dysfunction, skin temperature oscillations, local heating test, wavelet transform
Transmission detector for at-treatment QA

Delta^4 Discover

by ScandiDos

Confidence | Safety | Accuracy | Efficiency
With the future of radiation therapy trending towards increasingly complex treatment plans, including 4D treatments, hypofractionation and adaptive radiotherapy, the need for instantaneous plan approval and maximum accuracy during all stages of QA is greater than ever before.

To us, a solution includes both accuracy in determining the dose delivered to the patient but also efficiency and ease of use with minimal changes to the normal workflow at the clinic. It also includes the tools required for a physicist to find the cause of errors and discrepancies when they occur.

Our solution is the Delta4 Discover, a transmission detector that measures the transmission dose in the cleverest way, including minimal attenuation and minimal increase in skin dose to the patient without reducing treatment clearance.

With **Express Measure** — a feature of Delta4 Discover — the high-speed measurement system monitors all critical treatment parameters with no interaction or preparation required.

The Delta4 Discover has enabled the development of the **Delta4 Synthesis** which ensures delivered dose verification in the patient anatomy at-treatment by combining the 4D reference data of the Delta4 Phantom+ and Delta4 Discover. By easily adapting to changing clinic environments and advanced therapies, the Delta4 Discover delivers a complete solution.

The innovative Delta4 Discover transmission detector provides confidence and patient safety based on real time measurements. Its outstanding accuracy and ease of use assures the highest efficiency in your patient QA.
Session
Radiology and Roentgenology 2
NATIONAL SURVEY ON THE ACCURACY OF ACTIVITY MEASUREMENT PERFORMED WITH DOSE CALIBRATORS

M.Dimcheva¹, P.Trindev²

¹Department of Nuclear Medicine, Sofia Cancer Center, Sofia, Bulgaria; ²QC in Nuclear Medicine Consultant, Sofia, Bulgaria

Abstract

The main objective of this national survey was to provide data on the accuracy of activity measurements of the dose calibrators (DC) used in nuclear medicine departments in Bulgaria. In 2015 over a period of two months, measurements were performed on 25 DC in all 18 nuclear medicine departments in Bulgaria. The dose calibrators included in the survey were delivered in the last 37 years by 7 manufacturers. The tests were focused mainly on the accuracy and were carried out using two certified reference sources: Cs-137 (662 keV), with manufacturer serial number LB 165 and Ba-133 (356 keV) with manufacturer serial number KF 951. The results of the accuracy test for Cs-137 show deviations from the expected value in a wide range –20.5 % to +21.3 %, while for Ba-133, deviations are in the range from –5.2 % to +17.1 %. According to the National Regulation only 6 of 25 DC are in the range +5.5 %, 4 in the range +5 % and 3 of them, brand new, situated in one department. Bulgarian State Regulations require that deviation between measured and expected values must be within ±5 percent of the average. Errors greater than ±5 % in the interval from –20.5 % to +21.3 % were found in 18 of the 25 (DC). According to the results of this survey, the accuracy of dose calibrators does not meet the requirements of National Regulations and requires special attention and adequate response.

Key words: Dose calibrators, accuracy of activity measurement, calibration factors
Introduction

The main objective of this survey was to provide data on the performance of dose calibrators used in all nuclear medicine departments in Bulgaria. In particular we aimed to test the basic parameters of dose calibrators: accuracy and precision.

Materials and Methods

In 2015 over a period of two months, measurements were performed on 25 dose calibrators in all 18 nuclear medicine units. The dose calibrators included in the survey were delivered in the last 37 years by 7 manufacturers (Table 1)

Table 1. Dose Calibrators Tested

<table>
<thead>
<tr>
<th>Manufacturer</th>
<th>Model</th>
<th>Quantity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Biodex</td>
<td>Atomlab 500</td>
<td>1</td>
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<tr>
<td>Capintec</td>
<td>CRC®-15R</td>
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<td>PTW Freiburg GmbH</td>
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<td>Comecer</td>
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</tr>
<tr>
<td>Picker</td>
<td>Isotope Calibrator</td>
<td>2</td>
</tr>
<tr>
<td>Robotron</td>
<td>M 27013</td>
<td>1</td>
</tr>
</tbody>
</table>

Prerequisite for a correct measurement is a source with a valid certificate – i.e. with known activity. As a rule each dose calibrator should have his own control source in order to track its accuracy performance [2, 3]. Usually it is a $^{137}\text{Cs}$ source with a half life of 30 years.
We had a preliminary information that half of the control sources in Bulgaria do not have a certificate hence their activity is unknown. That is why we decided to carry out the test of all dose calibrators with one control source – $^{137}$Cs with reliable certificate (Figure 1). The approach with common source for all measurement has an additional advantage – real objective comparison among all dose calibrators.

For the purpose of the study was developed a unified form which contains data of a medical department, date of measurement, type and number of a dose calibrator, serial number of the local source and certificate number (if applicable) [3], tables for 20 measurements of each source. The top upper table contains the results of the control source $^{137}$Cs LB 165 measurement. Next tables are allocated for the measurements of the local control sources. Below each table are the results of the average, the standard deviation and the outcome of $\chi^2$ criterion (Figure 2)

![Figure 1. $^{137}$Cs control source](image1)

![Figure 2. Unified sample form](image2)
Results

ACCURACY. For most diagnostic and therapeutic applications it will be acceptable if the activity actually administered to a patient is within ±10% of the activity specified. In order that this intended overall accuracy can be achieved in practice, the tolerance of a calibration accuracy must be considerably smaller. Bulgarian State Regulations require that deviation between measured and expected values must be within ±5 % of the average of at least 10 measurements [1]. On the chart (Figure 3) the summarized results of the accuracy test are presented. The columns in blue present the percent error of measurements with the common source. Errors greater than ±5 % in the interval from +21.3 % to –20.5% were found in 18 of the 25 dose calibrators. It is interesting to note that the result which was close to the expected one (error of 0.3%) was delivered by the oldest (>35 years) dose calibrator – Picker and the two dose calibrators of manufacturer Comec recently installed.

Figure 3. Results from local measurement of the control source $^{137}$Cs LB 165 (columns in blue) and local source of $^{137}$Cs (columns in orange)

Columns in orange present the results of measurement of the local source with certificate – it means with known activity value. In some cases, the results obtained are similar with those of the common source, while in other cases there are clearly significant difference. The latter should also be examined in detail.

The most probable reason for these unfavorable results is the lack of preventive service maintenance. Expiry date of the guarantee of the most numerous dose calibrators Curiementor PTW, type 3 is 10 years, while they are in use more than 13 years. There are reasons to suspect that the accuracy problem originates from the decreased pressure of the gas in the ionization chamber but we are not able to check it out unfortunately.

PRECISION: $\chi^2$ criterion evaluates the reliability of the results of successive measurements of processes that are stochastic in nature, as in the case dose calibrators [2]. The estimated result for the accuracy criterion $\chi^2$ of 20 measurements is expected to be within the range of $11.7 < \chi^2 < 27.2$ confidence limits $0.90 > P > 0.10$. The results of all dose calibrators in $\chi^2$ criterion in our study were less than 1, which means that the variations are very small or devices are "too accurate." Or in other words, at first glance this criterion
seems not applicable in dose calibrators, which is strange as a fact. We asked for the reason for these strange results and reached the following explanation: The dose calibrator does not indicate the exact number of registered events rather its conversion to Curie or Becquerel. During the conversion process the number of registered events is rounded to 1 or 2 orders of magnitude which is fatal for $\chi^2$ criterion. This can be demonstrated by the following examples (Figure 4).

Calculated value of $\chi^2$ obtained from 20 measurements shown on the left table, obviously is within the limits of the range, indicating that the results belong to the Poisson distribution. If those 20 values are rounded to tenths, as shown in the right table and calculate $\chi^2$ for 20 values shown in black, the result of $\chi^2$ is completely different from that of the table on the left, which explains the results $\chi^2 < 1$ in dose calibrators.

\[
\begin{array}{cccc}
4054 & 4195 & 4269 & 4164 \\
4213 & 4145 & 4357 & 4262 \\
4231 & 4112 & 4191 & 4096 \\
4313 & 4154 & 4192 & 4210 \\
4096 & 4247 & 4093 & 4161 \\
\end{array}
\]  
\[
\begin{array}{cccc}
4054 & 4195 & 4269 & 4164 \\
4213 & 4145 & 4357 & 4262 \\
4231 & 4112 & 4191 & 4096 \\
4313 & 4154 & 4192 & 4210 \\
4096 & 4247 & 4093 & 4161 \\
\end{array}
\]

\[\bar{x} = 4195.75 \quad \chi^2 = 24.44 \]  
\[\bar{x} = 418.4 \quad \chi^2 = 2.63 \]

\[11.7 < \chi^2 < 27.2\]

Figure 4. Assessment $\chi^2$ criteria

The conclusion that can be drawn from the examination of this parameter is that the criterion $\chi^2$ is not applicable for dose calibrators.

Discussion

According to the results of the first national survey, the studied NM centers did not generally have acceptable situations in terms of the accuracy of activity measurement performed with dose calibrators. In addition, according to the data obtained in the study, more than 90% of nuclear medicine departments do not conduct tests for quality control of dose calibrators and do not record the results.

Conclusions

According to the results of this study, the accuracy of the dose calibrators does not meet the requirements of National Regulations and requires special attention and adequate
response – namely immediate calibration of dose calibrators and procurement of valid certificate for the control sources without certificate.

References:

1. Ordinance № 30 of October 31, 2005 on terms and conditions to ensure the protection of individuals in medical exposure, amended and supplemented State Gazette No 27/ 15.03 2013.
INCIDENTS AND ACCIDENTS IN IMAGING DEPARTMENTS. WHAT’S NEXT?

Virginia Tsapaki
Senior General of IOMP

X-rays are classified as a carcinogen by the World Health Organization's International Agency for Research on Cancer. Currently, experimental and epidemiological data do not support the proposition that there is a threshold radiation dose below which there is no increased risk of cancer. It is estimated that 0.4% of current cancers in the United States are due to computed tomography (CT) scanning performed in the past and that this may increase to as high as 1.5-2% with 2007 rates of CT usage. US Food and Drug Administration (FDA) estimates that exposure to 10 mSv from an imaging test would be expected to increase the risk of death from cancer by about 1 chance in 2000.

At the same time high dose X-ray imaging such as CT have boosted clinical applications of X-ray use. CT is currently considered as one of the most important imaging techniques of modern times. The introduction of multi-detector CT (MDCT) and CT fluoroscopy have further advanced CT applications by enabling interventional radiological (IR) procedures, which were traditionally performed using C-arm X-ray systems. However, a growing number of adverse events related to excessive CT radiation exposure, as well as its relation to elevated risk of radiation induced cancer are reported in the media.

Modern X-ray equipment together with improvement in techniques and devices have facilitated cardiologists and other physicians, pledging more successful clinical outcome, thus resulting in a profound change in the treatment of coronary heart disease and various periphery vessels. High radiation doses can very easily accumulate due to extended fluoroscopy times needed to monitor the devices to the area of interest and the large recording, there is also high risk of skin injuries to patients and occupational overexposure of the staff involved. Interventionalists are often unaware of the high radiation doses to which a patient's skin may be subjected, even with the use of modern, state of the art equipment. It continues to surprise many cardiologists, that radiation burns can occur that can be chronically and severely painful, not to mention that both operators and hospitals are often subjected to the legal action that follows such events. All these will be discussed and recommendations will be given to avoid such events.

- **Key words:** X-ray equipment, CT, MDCT, C-arm X-ray systems
TRACKING THE EFFECT OF OPTIMISATION IN A PAEDIATRIC RADIOLGY DEPARTMENT

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\textsuperscript{2}National Cardiology Hospital, Sofia, Bulgaria  
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\textsuperscript{4}University Hospital “St. Ekaterina”, Sofia, Bulgaria

Abstract

The purpose of this work is to evaluate the effect of optimisation of paediatric chest radiography applied in in a paediatric radiology department.

Optimised protocols including optimal exposure parameters and radiography technique were developed and recommended in 2011, based on patient size for different age groups. Data were analysed in four age groups: 1–12 months, 1–4, 5–9 and 10–15 y. The first survey performed immediately after the implementation of the optimised protocols showed decrease in KAP values in a factor of between 2 (from 8.06 to 3.65 \( \mu \text{Gy.m}^2 \)) and 5 (from 3.59 to 0.70 \( \mu \text{Gy.m}^2 \)) for different age groups. A new survey implemented 5 years after the utilisation of the optimised protocols showed 100 % utilization of the proposed optimized protocols. Additional decrease in KAP values was found by a factor of between 1.4 (from 0.7 to 0.5 \( \mu \text{Gy.m}^2 \)) and 3.6 (from 5.53 to 1.53 \( \mu \text{Gy.m}^2 \)) for different age groups. Image quality was assessed to be of sufficient diagnostic quality.

The survey demonstrated that the implementation of the proposed optimised protocols and radiography technique in the routine radiography practice lead to sustainable low doses to paediatric patients at good diagnostic quality.
Introduction

Paediatric x-ray optimisation is more challenging than adult optimization. The dose investigations for adult patients often relate to standard size patients of approximate weight of 70kg. For paediatric patients the optimal exposure parameters may vary significantly with the age and size of the child. Collection of paediatric data at all ages is a very challenging task affected by the low frequency of x-rays performed, with 11% of all x-ray examinations performed in Bulgaria in 2014 being associated with children [2]. The most commonly performed radiographic examination on children in Bulgaria is posteroanterior (PA)/anteroposterior (AP) chest examination with a frequency of about 13% [1, 2].

Two different studies had been performed in the period 2009-2011. The first authors’ study presented comparison of the important aspects of paediatric radiological practice and patient doses from chest X-ray examinations in different hospitals in Bulgaria [3, 4]. The second study presented an algorithm for the optimisation of paediatric chest radiography in a paediatric hospital with reduced patient doses but assuring sufficient image quality [4]. Five different age and weight-based optimised protocols including optimal exposure parameters and radiography technique were developed and recommended in 2011, based on the patient size for different age groups. One of the main goals of the previous studies was to encourage the radiographer to address the paediatric safety issues and the implementation of regular use of the improved radiography technique and the suggested optimal exposure parameters. Dose audit for paediatric patients is a key step in the optimisation of x-ray examinations. The purpose of this work is to track the effect of optimisation of paediatric chest radiography applied in the paediatric radiology department.

Materials and Methods

Data for 24 paediatric patients were recorded for a month using a questionnaire including information for patient age, height, weight, gender, exposure parameters, radiographic technique and displayed air kerma–area product (KAP) values. Measurements of KAP were performed with a KAP meter integrated in the X-ray system. All aspects of paediatric radiography practice were assessed and compared with the results from the study performed 4 years ago. Data were divided in four age groups: 1–12 months, 1–4, 5–9 and 10–15 y for the same radiographer working with the same X-ray system.

Results

The results from the patient audit performed 5 years after the utilisation of the optimised protocols showed 100% utilization of the proposed optimized protocols.

Image quality of chest AP/PA projections for each patient was evaluated by the same experienced paediatric radiologist and was assessed as “acceptable” for all the x-ray examinations. The earlier study showed that 17% of the images were assessed with not sufficient but still acceptable image quality due to wrong choice of protocol. The reason for such a result was the radiographer, who took into account only the patient’s age without considering the size. Five years later, the better radiographic experience led to correct choice of an optimised protocol, according to the combination of the individual size and age of each examined child.
The new audit showed that the automatic exposure control (AEC) was never used for children under 12 years leading to lower doses compared to an improper use of the AEC in 2011 when a child received two times higher doses. There is no data available about the chamber selection.

The antiscattering grid was used only for children able to cooperate and stand upright in front of the vertical stand – always for patients over the age of 4. Children, younger than 4 years, were examined in a supine (whenever possible – prone) position on the table, with a cassette over the table.

The new survey showed additional dose reduction to sensitive organs by means of shielding and better collimation compared to the previous study which showed worse collimation. The reason for the bad results was the lack of an experience of the radiographer in 2011.

Strong correlation was found between the tube voltage values and the patient age and weight – with correlation coefficient R2 of 0.85 and 0.77 respectively, compared to no correlation in the previous study. The dependence of the tube voltage values on patients’ age and weight are shown in Figure 1.

After the implementation of the optimised protocols for paediatric patients, exposure time less than 10 ms was used for 91% of the patients. The tracking of the effect of optimisation in the paediatric radiology department showed that exposure time less than 10 ms, recommended by European Guidelines EUR 16261, was used in 100% of the cases (Table 1) [5].
Table 1. Exposure parameters (exposure time and mAs product) before the optimisation process, after the implementation of the optimised protocols in 2011 and tracking the optimisation effect in 2016.

<table>
<thead>
<tr>
<th>Age group</th>
<th>X-ray unit</th>
<th>Exposure parameters</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>m</td>
</tr>
<tr>
<td>1-12 m</td>
<td>Before optimisation</td>
<td>12</td>
</tr>
<tr>
<td></td>
<td>After optimization 2011</td>
<td>5</td>
</tr>
<tr>
<td></td>
<td>After optimization 2016</td>
<td>5</td>
</tr>
<tr>
<td>1-4 y</td>
<td>Before optimisation</td>
<td>11</td>
</tr>
<tr>
<td></td>
<td>After optimization 2011</td>
<td>5</td>
</tr>
<tr>
<td></td>
<td>After optimization 2016</td>
<td>5</td>
</tr>
<tr>
<td>5-9 y</td>
<td>Before optimisation</td>
<td>16</td>
</tr>
<tr>
<td></td>
<td>After optimization 2011</td>
<td>5</td>
</tr>
<tr>
<td></td>
<td>After optimization 2016</td>
<td>5</td>
</tr>
<tr>
<td>10-15 y</td>
<td>Before optimisation</td>
<td>24</td>
</tr>
<tr>
<td></td>
<td>After optimization 2011</td>
<td>8</td>
</tr>
<tr>
<td></td>
<td>After optimization 2016</td>
<td>5</td>
</tr>
</tbody>
</table>

MIN - minimum, MAX - maximum, AV - average

The first survey performed immediately after the implementation of the optimised protocols showed decrease in KAP values in a factor of between 2 (from 8.06 to 3.65 μGy.m2) and 5 (from 3.59 to 0.70 μGy.m2) in the different age groups (fig. 2). The dose audit according to tracking the effect of optimisation in 2016 showed additional decrease in KAP values by a factor of between 1.4 (from 0.7 to 0.5 μGy.m2) and 3.6 (from 5.53 to 1.53 μGy.m2) in the different age groups. The results are shown on fig. 2. The implementation of good radiology practice is also expressed as no significant difference between the minimum and maximum KAP values in 2016 for all age groups compared to the big difference before the optimisation process. The highest decrease in KAP values was in age group (10-15 y). The comparison for the KAP values between the implementation of the optimised protocols and 5 years after their routine use resulted in total decrease in a factor of between 3.3 and 9.5. Image quality was assessed to be of sufficient diagnostic quality.
Figure 2. KAP values for all age groups before and after the optimization in 2011 and tracking the effect of optimization in 2016.
Conclusions

The survey demonstrated that the implementation of the proposed optimised protocols and radiography technique in the routine radiography practice lead to sustainable low doses to paediatric patients at good diagnostic image quality. The patient dose for one of the age groups was decreased more than 9 times.

References:

PILOT STUDY OF PATIENT DOSES FROM DIGITAL BREAST
TOMOSYNTHESIS IN BULGARIA

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Abstract

The first systems for Digital Breast Tomosynthesis (DBT) were installed in Bulgaria in 2015. This study aims to perform pilot estimation of patient doses from examinations on two DBT systems – GE Senograph Essential and IMS Giotto Tomo.

Incident air kerma (IAK) and mean glandular dose (MGD) were determined applying the method proposed in the Protocol for the Quality Control of the Physical and Technical Aspects of Digital Breast Tomosynthesis Systems (PQCDBT). Patient data for 76 patients on the first system and 92 patients on the second system were retrospectively collected from the picture archiving and communication systems (PACS) of the hospitals. The total number of exposures considered of both breasts and all projections on the first system was 300, and the respective number on the second system was 259, in both planar and DBT modes of operation. IAK and MGD were also estimated for standard PMMA phantom with thicknesses from 20 to 60 mm.

The mean compressed breast thickness (CBT) for patients’ samples for both modes of operation on the first system was 51 mm, mean IAK and MGD per exposure for the planar mode were 6.3 mGy and 1.5 mGy respectively. For the DBT mode these data were 7.5 mGy and 1.8 mGy. For the second system mean CBT, IAK and MGD for planar and DBT modes were, as follows: 62 mm, 3.6 mGy and 1 mGy; 52 mm, 6.5 mGy and 2 mGy.

Patient doses in the planar mode were about 43 % higher on the first system in comparison to the second one, but in the DBT mode MGD was almost equal for both systems, within the uncertainty of the estimations. IAK and MGD were very similar for both modes of operation on the first system and about two times higher in the DBT mode compared to the planar mode on the second system. For both systems MGD for PMMA were below the published in the PQCDBT reference values. Comparison with previous studies for film-screen mammography in the country showed decrease in the dose levels with the introduction of the new digital technology. Our results are similar to published in literature.

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Introduction

Breast cancer is the most common oncological disease among women in Bulgaria and in developed countries [1, 2]. There is strong evidence that diagnosis at early stage significantly improves the survival rate [3]. Several studies proved the key role of mammography screening, leading to 20-30% or even higher reduction rate of breast cancer mortality [4-8]. Although initially film-screen mammography was established as the “gold standard” in screening programmes, digital mammography also proved to be at least as good as film-screen mammography [9-12]. In the late 1990s the development of the digital detectors technology and the introduction of the flat panels to the market revived the old idea of tomographic imaging and a new imaging method, the tomosynthesis, was developed [13]. One of its applications is the digital breast tomosynthesis (DBT). Usually the DBT system is a digital mammography system, able to perform standard two-dimensional (2D) images, and also having the possibility to perform exposures of the breast at different limited angles through X-ray tube movement around the breast, either step-and-shoot or continuous [14]. The projections acquired are then reconstructed and “quasi-3D” images are obtained [15]. The first approved in 2011 by the U.S. Food and Drug Administration DBT system was the Selenia Dimensions 3D System of Hologic, Inc. Since then several manufacturers produce DBT systems. Many authors study the place of this method in mammography screening. The initial results are promising. Some studies are focused on the place of DBT performed together with 2D mammography, while others consider the use of DBT alone, or DBT in one view and 2D in another view, compared to 2-view 2D digital mammography for the whole examination. Some studies explore the potential of using the synthetic 2D images, provided by some DBT systems, as a supplement to the 3D imaging instead of real 2D examination. In general, increase in the cancer detection rate, reduction in recall rate, improved sensitivity and specificity were reported after the introduction of DBT [16-24].

Very important aspect of the application of imaging methods using ionizing radiation, especially for screening, is patient exposure, related to some carcinogenic risk. The International Commission on Radiological Protection (ICRP) recommends the use of the quantity mean glandular dose (MGD) for estimation of radiation risk in mammography [25]. MGD represents the mean absorbed dose to the glandular tissue in the breast. It depends on the X-ray spectrum, the mammography system technical parameters, the thickness and the composition of the breast. MGD cannot be measured directly. The widely adopted approach to determine MGD is to estimate a measurable quantity and to calculate MGD through conversion coefficients, based on Monte Carlo calculations. Two formalisms are accepted worldwide. The American method, used in the USA, Canadian and Australian protocols [26-29], is based on the measurement of entrance skin exposure (ESE) and calculation of MGD through the published by Wu et al. and Stanton et al. conversion coefficients [30-32]. The European approach, adopted also by the International Atomic Energy Agency (IAEA) [33-37], is based on the measurement of incident air kerma (IAK) and the coefficients of David Dance and co-workers [38-40]. Both formalisms are very similar, but based on slightly differing breast models. The introduction of DBT, performed at different geometry than 2D mammography, leads to extension of both American and European dosimetry protocols and the provision of new groups of coefficients for tomosynthesis, applied supplementary to the already existing coefficients [41-44].

The first DBT systems were installed in Bulgaria in 2015. To our knowledge, there are four systems under operation or undergoing licensing process in the country thus far. This study aims to perform pilot estimation of patient doses from examinations on two DBT systems.
Materials and Methods

The systems included in the study were Senograph Essential/SenoClaire (GE Healthcare), denoted as System 1 in this text and Giotto Tomo (IMS), denoted as System 2. These systems have the possibility to perform both 2D mammography and DBT. The method proposed in the Protocol for the Quality Control of the Physical and Technical Aspects of Digital Breast Tomosynthesis Systems (PQCDBT), based on the European formalism, was used for determination of IAK and MGD [45]. Radiation output and half value layer (HVL) were estimated for all clinically used anode/filter (A/F) and tube voltage (kV) values, either by direct measurement or by calculation with the “Template_EFOMP_MammoWG_DR” Microsoft Excel worksheet of the Protocol of the EFOMP Mammo Working Group [46], performing calculations based on the parametric method, proposed by Robson [47]. Measurements on System 1 were performed with multimeter Accu-Gold+ (Radcal) and solid state detector AGMS-DM+. The measurements were performed in 2D mode and the same data were used for the calculation of patient doses in both 2D and DBT modes, because it was shown elsewhere, that tube output and HVL have the same values in both modes of operation for this model of equipment [48]. Ionization chamber T34069 (6 cm$^3$ sensitive volume) and electrometer Unidos (PTW Freiburg) were used on System 2. Comparison was performed between 2D and 3D modes of operation, taking into account the small angular dependence of the ionization chamber indication (≤3%). Differences of tube output in both modes of operation were within 0.7%, falling within the uncertainty of the estimation. Consecutively all calculations on this system were performed based on tube output measurements in 2D mode. The instruments used on both systems had the relevant calibrations for mammography beams.

Patient data were retrospectively collected from the picture archiving and communication systems (PACS) of the hospitals. The data collected included patient age, projection, compressed breast thickness (CBT), exposure parameters – A/F, kV, tube current-exposure time product (mAs) and indication of the dose, estimated by the system. IAK for each exposure was calculated by multiplying the tube output values for the A/F, kV used for the patient exposure, by the mAs, and applying inverse square law correction for breast thickness. MGD per exposure in 2D mode was calculated through multiplication of IAK by the relevant conversion coefficients, provided in separate tables [34, 45]:

$$\text{MGD}_{2D} = \text{IAK}.g.c.s$$

The $g$-coefficients convert IAK to MGD for a breast of glandularity 50%. The $c$-coefficients correct for any difference in breast composition from 50% glandularity. They are provided for the age groups 40-49 and 50-64 years, subject to breast screening programmes in the UK. Both $g$- and $c$-coefficients are HVL and CBT dependent. And $s$- is A/F dependent spectral correction factor, taking into account the different types of spectra used. For the DBT mode also $T$-factors, which are CBT dependent, are provided for the systems, included in the present study [45], and MGD was determined using the following formula:

$$\text{MGD}_{DBT} = \text{IAK}.g.c.s.T$$

Linear interpolation was applied to values of the $g$- and $c$- coefficients and $T$-factors, falling between the tabular values. Patients younger than 40 years were considered belonging to the 40-49 group and patients older than 64 were included in the 50-64 group for the choice of $c$-coefficient. MGD per patient was calculated, summing MGD per
exposure from all views, averaging over both breasts. In the rare cases when only one breast was examined, the doses from both views were only summed.

IAK and MGD were also estimated for standard polymethyl methacrylate (PMMA) phantom with thicknesses from 20 to 60-70 mm, using the same formalism and the coefficients provided for PMMA [45].

Results

On System 1 the patients were receiving either 2D mammogram (56 patients) or DBT (20 patients), depending on radiologist’s judgement, always of both breasts in two views: mediolateral oblique (MLO) and craniocaudal (CC). Exception was made for two patients with DBT, having examination of only one breast. All 55 patients considered on System 2 had 2D mammography of both breasts in MLO and CC views, and according to radiologist’s preference, 37 of them had later (usually the next day) 3D examination of one of the breasts in one view (2 patients had 2 views of one breast). The total number of exposures considered of both breasts and all views on the first system was 300 (224 in 2D and 76 in 3D), and the respective number on the second system was 259 (220 in 2D and 39 in 3D). Histograms of the age distributions of patients receiving 2D mammography and DBT are presented on Figures 1 and 2 respectively.

![Age distribution, 2D](image)

Figure 1. Age distribution of patients, undergoing 2D mammography, on System 1 and System 2.

Patients with 2D mammography in the age group below 49 were 32 % on System 1 and 27 % on System 2, while the others were classified in the age group above 50. These data for DBT, for women younger than 49 years, are 65% on System 1 and 32 % on System 2. The approach chosen by the radiologists working on System 1 was to advice younger women with denser breasts to perform DBT, which explains the higher percentage of young women performing DBT on this system. On System 2 rather patients with some findings were recalled for DBT after examination of the mammograms.
Figure 2. Age distribution of patients, undergoing DBT, on System 1 and System 2.

Histograms of CBT distributions in 5 mm bands of patient’s samples on both systems are presented on Figures 3 and 4 for 2D and DBT respectively. Data were separated by view (MLO or CC), because it influences both the thickness and MGD. In MLO view the pectoral muscle is present in the X-ray beam, leading to usually higher thickness and dose.

Figure 3. Histogram of CBT distribution of patients, undergoing 2D mammography on both systems. Data are separately presented for MLO and CC views.
IAK for 2D imaging on System 1 varied between 2.53 and 14.06 mGy, mean 6.31 mGy, while on System 2 it was between 2.09 and 12.93 mGy, mean 3.63 mGy. For DBT IAK on System 1 was between 3.32 mGy and 20.85 mGy, mean 7.46 mGy, and on System 2 it varied between 3.27 mGy and 19.26 mGy, mean 6.47 mGy.

Figures 5 and 6 show the distributions of MGD per exposure and per view, in 0.2 mGy bands, for 2D and DBT respectively. The relative expanded uncertainty (k = 2) in the determination of MGD was found to be 15 % for both systems. The different distribution of glandular tissue within the breast was not taken into account in these estimations.
Figure 6. Histogram of MGD distribution per exposure of patients, undergoing DBT on both systems. Data are separately presented for MLO and CC views.

Similar distribution of MGD per patient is shown on Figure 7 for 2D examinations. Such a graph was not prepared for DBT, because it would not be representative for two reasons. The first is the small number of patients (20) with DBT on System 1, functioning only several months. All data available for this type of examination were retrieved. The second reason is that contrary to System 1, where almost all patients had exposures in DBT of both breast in 2 views (4 exposures per patient, prophylactic examination), on System 2 most of the patients received only one view exam of one breast (1 exposure per patient, in fact diagnostic examination after 2D mammography), making data for the total MGD per patient incomparable.

Figure 7. Histogram of MGD distribution per patient, of women, undergoing 2D mammography on both systems.
Statistical data on CBT, MGD per exposure and MGD per patient are presented for 2D mammography in Table 1, and for DBT in Table 2, respectively. Mean values of the quantities, standard deviations $\sigma$, minimum and maximum values are included. The numbers of exposures and patients are also presented. Because of the skewed nature of the distributions (Figures 5, 6 and 7), median values, 1st and 3rd quartiles were also added as better descriptors.

Table 1. Statistical data on CBT, MGD per exposure and MGD per woman for patients, undergoing 2D mammography.

<table>
<thead>
<tr>
<th>System / view</th>
<th>No of exposures</th>
<th>Compressed breast thickness (mm)</th>
<th>MGD per exposure (mGy)</th>
<th>No of patients</th>
<th>MGD per patient (mGy)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Mean ± $\sigma$ (min, max)</td>
<td>Median (1st quartile, 3rd quartile)</td>
<td>Mean ± $\sigma$ (min, max)</td>
<td>Median (1st quartile, 3rd quartile)</td>
</tr>
<tr>
<td>1 / all</td>
<td>224</td>
<td>51.4 ± 12.1 (22, 78)</td>
<td>53 (43, 60)</td>
<td>1.52 ± 0.32 (0.93, 2.92)</td>
<td>1.48 (1.26, 1.71)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>1.56 ± 0.34 (1.01, 2.92)</td>
<td>1.50 (1.29, 1.75)</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>1.47 ± 0.30 (0.93, 2.46)</td>
<td>1.46 (1.24, 1.65)</td>
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<tr>
<td></td>
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<td></td>
<td></td>
<td>1.46 ± 0.30 (0.93, 2.46)</td>
<td>1.46 (1.24, 1.65)</td>
</tr>
<tr>
<td>1 / MLO</td>
<td>112</td>
<td>52.8 ± 12.8 (22, 78)</td>
<td>54 (44, 62)</td>
<td>1.57 ± 0.34 (1.01, 2.92)</td>
<td>1.50 (1.29, 1.75)</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>1.47 ± 0.30 (0.93, 2.46)</td>
<td>1.46 (1.24, 1.65)</td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td>1.47 ± 0.30 (0.93, 2.46)</td>
<td>1.46 (1.24, 1.65)</td>
</tr>
<tr>
<td>1 / CC</td>
<td>112</td>
<td>50.0 ± 11.3 (22, 75)</td>
<td>52 (42, 57)</td>
<td>1.47 ± 0.30 (0.93, 2.46)</td>
<td>1.46 (1.24, 1.65)</td>
</tr>
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<td></td>
<td></td>
<td></td>
<td></td>
<td>1.47 ± 0.30 (0.93, 2.46)</td>
<td>1.46 (1.24, 1.65)</td>
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<td>1.47 ± 0.30 (0.93, 2.46)</td>
<td>1.46 (1.24, 1.65)</td>
</tr>
<tr>
<td>2 / all/AEC</td>
<td>88</td>
<td>60.2 ± 10.6 (40, 86)</td>
<td>59 (52, 67)</td>
<td>1.17 ± 0.45 (0.59, 3.46)</td>
<td>1.10 (0.81, 1.38)</td>
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<td>1.12 ± 0.54 (0.60, 3.46)</td>
<td>1.12 (0.81, 1.41)</td>
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<td>1.12 ± 0.54 (0.60, 3.46)</td>
<td>1.12 (0.81, 1.41)</td>
</tr>
<tr>
<td>2 / MLO AEC</td>
<td>44</td>
<td>64.2 ± 11.2 (40, 86)</td>
<td>64 (55, 71)</td>
<td>1.21 ± 0.54 (0.60, 3.46)</td>
<td>1.12 (0.81, 1.41)</td>
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<td>1.12 ± 0.54 (0.60, 3.46)</td>
<td>1.12 (0.81, 1.41)</td>
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<td></td>
<td>1.12 ± 0.54 (0.60, 3.46)</td>
<td>1.12 (0.81, 1.41)</td>
</tr>
<tr>
<td>2 / CC AEC</td>
<td>44</td>
<td>56.2 ± 8.2 (44, 80)</td>
<td>57 (50, 59)</td>
<td>1.12 ± 0.33 (0.63, 2.15)</td>
<td>1.09 (0.86, 1.30)</td>
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<td>1.12 ± 0.33 (0.63, 2.15)</td>
<td>1.09 (0.86, 1.30)</td>
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<td></td>
<td>1.12 ± 0.33 (0.63, 2.15)</td>
<td>1.09 (0.86, 1.30)</td>
</tr>
<tr>
<td>2 / all/manual</td>
<td>132</td>
<td>62.3 ± 10.7 (34, 86)</td>
<td>64 (55, 70)</td>
<td>0.88 ± 0.25 (0.48, 1.94)</td>
<td>0.81 (0.74, 0.96)</td>
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<td></td>
<td>0.88 ± 0.25 (0.48, 1.94)</td>
<td>0.81 (0.74, 0.96)</td>
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<td></td>
<td>0.88 ± 0.25 (0.48, 1.94)</td>
<td>0.81 (0.74, 0.96)</td>
</tr>
<tr>
<td>2 / MLO manual</td>
<td>66</td>
<td>65.1 ± 11.4 (34, 86)</td>
<td>67 (57, 72)</td>
<td>0.86 ± 0.26 (0.48, 1.94)</td>
<td>0.79 (0.73, 0.94)</td>
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<td>0.86 ± 0.26 (0.48, 1.94)</td>
<td>0.79 (0.73, 0.94)</td>
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<td></td>
<td>0.86 ± 0.26 (0.48, 1.94)</td>
<td>0.79 (0.73, 0.94)</td>
</tr>
<tr>
<td>2 / CC manual</td>
<td>66</td>
<td>59.5 ± 9.2 (39, 79)</td>
<td>62 (53, 66)</td>
<td>0.90 ± 0.24 (0.51, 1.72)</td>
<td>0.85 (0.79, 0.97)</td>
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<td></td>
<td>0.90 ± 0.24 (0.51, 1.72)</td>
<td>0.85 (0.79, 0.97)</td>
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<td></td>
<td>0.90 ± 0.24 (0.51, 1.72)</td>
<td>0.85 (0.79, 0.97)</td>
</tr>
</tbody>
</table>

84
Table 2. Statistical data on CBT, MGD per exposure and MGD per woman for patients, undergoing DBT.

<table>
<thead>
<tr>
<th>System</th>
<th>No of exposures</th>
<th>Compressed breast thickness (mm)</th>
<th>MGD per exposure (mGy)</th>
<th>No of patients</th>
<th>MGD per patient (mGy)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Mean ± σ (min, max)</td>
<td>Median (1st quartile, 3rd quartile)</td>
<td>Median (1st quartile, 3rd quartile)</td>
<td>Mean ± σ (min, max)</td>
</tr>
<tr>
<td>1 - all</td>
<td>76</td>
<td>50.5 ± 12.8 (28, 82)</td>
<td>1.77 ± 0.62 (1.03, 3.75)</td>
<td>1.59 (1.38, 1.95)</td>
<td>20</td>
</tr>
<tr>
<td></td>
<td></td>
<td>48 (42, 55)</td>
<td></td>
<td></td>
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<tr>
<td>MLO</td>
<td>38</td>
<td>50.0 ± 12.3 (29, 82)</td>
<td>1.75 ± 0.58 (1.12, 3.53)</td>
<td>1.54 (1.00, 1.96)</td>
<td>-</td>
</tr>
<tr>
<td>CC</td>
<td>38</td>
<td>50.9 ± 13.5 (28, 81)</td>
<td>1.80 ± 0.65 (1.03, 3.75)</td>
<td>1.60 (1.00, 1.93)</td>
<td>-</td>
</tr>
<tr>
<td>2 - all</td>
<td>39</td>
<td>52.1 ± 12.2 (29, 84)</td>
<td>1.96 ± 0.76 (1.28, 4.88)</td>
<td>1.75 (1.51, 2.18)</td>
<td>37</td>
</tr>
<tr>
<td></td>
<td></td>
<td>52 (44, 60)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MLO</td>
<td>15</td>
<td>57.9 ± 13.8 (31, 84)</td>
<td>2.23 ± 1.03 (1.28, 4.88)</td>
<td>1.91 (1.55, 2.40)</td>
<td>-</td>
</tr>
<tr>
<td>CC</td>
<td>24</td>
<td>48.5 ± 9.8 (29, 67)</td>
<td>1.79 ± 0.48 (1.28, 2.97)</td>
<td>1.68 (1.46, 1.99)</td>
<td>-</td>
</tr>
</tbody>
</table>

On System 2 60% of the patients had 2D images performed in manual mode, due to the judgement of the radiographers, in order to apply less compression force. The system is not allowing exposure in automatic mode (AEC) without adequate compression force. Data on exposures in manual and automatic modes of operation are presented separately. The mean CBT ± σ on System 1 is 51.4 ± 12.1 mm for 2D exams, with slightly higher value for the MLO view (52.8 ± 12.8 mm, vs 50.0 ± 11.3 mm for CC view), and mean MGD ± σ per exposure is 1.52 ± 0.32 mGy. On System 2 the mean CBT for 2D is higher with value of 60.2 ± 10.6 mm in AEC and 62.3 ± 10.7 mm in manual mode. In MLO views again the values are higher. Mean MGD per exposure is 1.17 ± 0.45 mGy in automatic and 0.88 ± 0.25 mGy in manual mode. The lower mean MGD on System 2, manual mode, is most probably due to the subjective choice of exposure parameters by the radiographers. But even in AEC mode, doses on System 2 are in general lower than on System 1. A reason for that observation could be the A/F combinations, used on both systems. On System 1 Molybdenum/Molybdenum (Mo/Mo), Molybdenum/Rhodium (Mo/Rh) or Rhodium/Rhodium (Rh/Rh) combinations are used. The most frequently used combination (74% of all cases) is Rh/Rh, and tube voltage with that combination is 29 kV in 52% of cases. On System 2 the combination used is Tungsten/Silver (W/Ag) for all exposures, with 28 kV in 64% of the cases, 29 kV in 13%, and higher kV values up to 34 kV in the other 23%. The W/Ag combination is providing higher energy spectrum, related to less absorption of X-rays in the breast. This is confirmed by the HVL values measured on both systems. On System 1 HVL varied between 0.33 and 0.46 mm Al (the modal value is 0.43 mm Al), while on System 2 HVL was between 0.53 and 0.63 mm Al (modal value 0.56 mm Al). Figures 8 and 9 present MGD per exposure as a function of CBT for 2D imaging and DBT respectively.
The trend of higher doses on System 2 in AEC mode (magenta colour), compared to the manual mode (in pink) is well seen (Figure 8). Radiologists are satisfied by image quality in both cases. In general doses on System 1 (Figure 8, blue colour) are higher in 2D imaging for a given CBT, compared to System 2. However for DBT this is not the case anymore (Figure 9). Doses at particular CBT from both systems are similar. The mean MGD on System 1 in DBT is $1.77 \pm 0.62$ mGy (mean CBT $50.5 \pm 12.8$ mm), while on System 2 mean MGD is $1.96 \pm 0.76$ mGy (mean CBT $52.1 \pm 12.2$ mm).

Comparison with previous study on 5 film-screen (FS) mammography systems in the country showed decrease of the dose levels with the introduction of the new digital technology. The previous study reported mean ± standard deviation of MGD per exposure to be $1.2 \pm 0.6$ mGy, $1.8 \pm 0.7$ mGy, $2.0 \pm 0.9$ mGy, $2.4 \pm 1.6$ mGy and $2.8 \pm 1.2$ mGy on the 5 systems, respectively [49, 50]. Only the first of these values is lower than the estimated one in this survey.
on System 1 for 2D mode (1.52 ± 0.32 mGy), but it is within the uncertainty of the estimation, and none is lower than the values on System 2 for 2D (1.17 ± 0.45 mGy), AEC mode (Table 1). Even for DBT the values from the present study are in the middle of the range for FS mammography. Paulis and co-workers performed a study of patient doses on the same kind of equipment as System 1 from 236 examinations, including both 2D and DBT per each patient [48]. They reported mean MGD ± σ per exposure to be 1.62 ± 0.55 mGy from 2D and 1.49 ± 0.36 mGy from 3D examination. These data are comparable with the data from System 1 in the present study (Tables 1 and 2), with mean MGD of 1.77 mGy from 3D imaging slightly higher in our case. These data on System 2 are lower for 2D (1.17 mGy mean MGD in AEC) and higher for DBT (1.96 mGy). Shin et al. reported patient doses from combined 2D mammography and DBT for each patient, for the Selenia Dimensions System (Hologic), with the MGD data retrieved from the Digital Imaging and Communications in Medicine (DICOM) headers of the images [51]. Mean MGD from 2D exposure was found to be 1.63 mGy, and from DBT it was 1.74 mGy, also comparable to the present study. Cavagnetto et al. reported mean MGD from a sample of 300 mammograms 1.31 mGy for 2D, and 2.56 mGy for DBT, with mean CBT 58 mm, for the Selenia Dimensions System [52]. All patients in that study had both 2D and DBT. Dose estimations are higher than ours for the DBT mode, and for the 2D mode the values fall between the calculated on both systems in our study.

Results from phantom measurements on both systems are presented in Table 3. The chosen by the AEC of the systems spectra (A/F, kV) are included, as well as IAK and MGD in 2D and DBT modes, percentage differences of MGD between the two modes of operation per system, and also the acceptable and achievable levels for MGD, proposed in the PQCDBT [45]. Only the acceptable levels are applicable for DBT. The relative expanded uncertainty (k = 2) of IAK and MGD from phantom measurements was 7 % and 9 % respectively. Each value in the table is included with its uncertainty.

Table 3. Dosimetry data from exposures of PMMA phantom, percentage differences of MGD between the 2D and DBT modes, acceptable and achievable levels for MGD, phantom measurements [45]. Only the acceptable levels apply for DBT.

<table>
<thead>
<tr>
<th>PMMA (cm)</th>
<th>A/F kV</th>
<th>IAK (mGy)</th>
<th>MGD (mGy)</th>
<th>% difference between 2D and 3D MGD</th>
<th>Acceptable level (mGy)</th>
<th>Achievable level (mGy)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
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<tr>
<td>System 1</td>
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<tr>
<td>Mammography</td>
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<tr>
<td>20</td>
<td>Mo/Mo 26</td>
<td>2.68 ± 0.19</td>
<td>0.97 ± 0.09</td>
<td>2.93 ± 0.21</td>
<td>1.05 ± 0.09</td>
<td>8.3</td>
</tr>
<tr>
<td>30</td>
<td>Mo/Rh 27</td>
<td>3.42 ± 0.24</td>
<td>1.07 ± 0.10</td>
<td>2.88 ± 0.20</td>
<td>0.99 ± 0.09</td>
<td>-7.7</td>
</tr>
<tr>
<td>40</td>
<td>Mo/Rh 28</td>
<td>5.37 ± 0.38</td>
<td>1.62 ± 0.15</td>
<td>5.52 ± 0.32</td>
<td>1.22 ± 0.11</td>
<td>-24.5</td>
</tr>
<tr>
<td>45</td>
<td>Mo/Rh 28</td>
<td>7.22 ± 0.50</td>
<td>1.64 ± 0.15</td>
<td>5.23 ± 0.37</td>
<td>1.28 ± 0.12</td>
<td>-22.0</td>
</tr>
<tr>
<td>50</td>
<td>Rh/Rh 29</td>
<td>7.19 ± 0.50</td>
<td>1.62 ± 0.15</td>
<td>7.28 ± 0.51</td>
<td>1.62 ± 0.15</td>
<td>0.1</td>
</tr>
<tr>
<td>60</td>
<td>Rh/Rh 31</td>
<td>8.01 ± 0.56</td>
<td>1.62 ± 0.15</td>
<td>10.76 ± 0.75</td>
<td>2.15 ± 0.19</td>
<td>32.6</td>
</tr>
</tbody>
</table>
These data confirm the lower doses on System 2 in 2D mode for the thinner phantom thicknesses (20-50 mm), but for 60 mm PMMA MGD on System 1 is lower, 1.62 ± 0.15 mGy, compared to 2.15 ± 0.19 mGy on System 2. In DBT mode MGD is lower (except for 20 mm) on System 1. The dose saving effect on this system is more pronounced for thicker PMMA.

The acceptable levels are not exceeded in any system, taking into account the uncertainty of the measurements. The achievable levels are exceeded on System 1 for 20 mm PMMA in 2D mode.

Dance et al. estimated MGD on Hologic Selenia Dimensions for PMMA for thicknesses of 20, 30, 40, 45, 50, 60, and 70 mm to be 0.60, 0.84, 1.19, 1.44, 2.03, 2.74 and 3.12 mGy respectively in 2D mode, and 0.92, 1.13, 1.58, 2.08, 2.52, 3.77 and 4.65 mGy respectively in 3D mode [53]. The reported in the same paper MGD for the Siemens Inspiration DBT system, for the same thicknesses of PMMA, are as follows: 0.47, 0.63, 0.90, 1.03, 1.28, 1.70, and 2.17 mGy for 2D, and 0.91, 1.20, 1.63, 1.86, 2.13, 2.80, and 3.46 mGy for DBT respectively. Comparison with data in Table 3 show that our results are in line with the reported in that study.

Comparisons were performed between the calculated and displayed values of MGD. On System 1 they differed between -21 % and 29 %, mean 5 % for 2D imaging, and from -31 % to 5 %, mean -8 % for DBT. On System 2 the differences were between -23 % and 57 %, mean 1 % for 2D, and between -12 % and 17 %, mean 3 % for DBT. Doses on System 1 are calculated based on the American formalism [54], and System 2 provides dose estimations based on the European formalism [55]. Some differences between the measurement result and the displayed value on System 1 may arise from the estimation of ESE, determined from calibrated model that could differ for the particular mammography system. Similarly, HVL values used for the choice of conversion coefficients on System 2 are typical values for the given model of equipment and not measurements on the particular system, which could influence the result of displayed MGD calculation. Also, the AEC of this system automatically compensates for tube aging, and IAK is calibrated by the system engineers once per year, that could introduce some differences too. All these details are related to Giotto Tomo only, and the newest products do not entirely share the same features [55]. Both systems do not apply the special conversion factors for the DBT mode (neither European nor American), but adopt the value of 1 instead. Furthermore, we used the European formalism in our calculations, but it is related to some limitations in dose estimations. American and European approaches use slightly different breast models. Both are based on 50:50 adipose/glandular content, the European consists of central region with 40 mm thickness, surrounded by 5 mm adipose tissue, while the American has 42 mm total
thickness and external skin layer [26, 33, 43]. Yaffe et al. reported that the 50:50 adipose/glandular content assumption is not realistic [56]. Additional coefficients are provided for 1%, 25%, 50%, 75% and 100% glandular content in the American, and age dependent glandularity in the European formalism. The main source of uncertainty in the estimation of MGD is, from one hand, the difference in the conditions for the Monte Carlo simulations in the determination of the conversion coefficients, that are found to vary between 7% and 19% [57]. On the other hand, the glandular tissue content and its distribution within the breast strongly influences the estimated conversion coefficients and hence MGD, with up to 59% difference compared to standard values, according to some authors [58, 59]. Displayed calculations of MGD on System 2 are based on the age dependent c-factors for the age group 50-64 in both 2D and 3D modes [55]. The MGD on System 1 in 2D mode is determined based on the glandular content of the breast, estimated by the AEC, while in 3D mode the conventional glandularity, corresponding to the CBT according to Dance et al. is used [39, 60]. We performed separate estimations of MGD from 2D imaging on System 1, also taking into account the percentage of glandular content, estimated by the system and included in the DICOM header of the images. For that purpose tables with c-coefficients, provided for glandularities 0.1%, 25%, 50%, 75% and 100% were used instead of the 40-49 and 50-64 standard age tables [39]. Linear interpolation was applied to values between the tabular data. Differences between displayed and calculated values after calculation taking into account the glandular content, estimated by the AEC, decreased to the interval from -7% to 20%.

The measurement procedure of IAK/ESE may also influence the result depending on the place of the compression paddle and the type of instrument used. The American procedure states measurement of ESE with the dosimetry detector beside the standard phantom of the American College of Radiology, while in the European case IAK/tube output is measured with the compression paddle in contact with the detector [26, 34]. It has been shown that depending on whether solid state dosimeter or ionization chamber is used, additional 2% to 10% of uncertainty in the measurement result will be introduced by the forward scatter radiation in this measurement condition [61-65]. That could also contribute to the observed differences between displayed and estimated by us values.

Conclusions

A pilot estimation of patient exposures from DBT and 2D digital mammography was performed on two systems in Bulgaria. The method proposed in the PQCDBT was found applicable, although the limitations of the formalism proposed should be taken into account. The mean MGD per exposure for the whole patient sample on System 1 from 2D examination was found to be 1.52 ± 0.32 mGy, and for DBT it was 1.77 ± 0.62 mGy. These data on System 2 were 1.17 ± 0.45 mGy in automatic and 0.88 ± 0.25 mGy in manual mode, 2D examination, and 1.96 ± 0.76 mGy for DBT. The doses from both 2D and DBT mammography examinations were found comparable or lower than reported by other similar studies, and lower than FS data in our country from previous studies. Although MGD values shown by the DBT systems on the diagnostic workstation displays differ somehow from the calculated values, they could be used in case of broad (e.g. national) surveys, aimed at elaboration of diagnostic reference levels.
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Session
Biophysics
Synthetic cationic lipids, which form stable complexes (lipoplexes) with polyanionic nucleic acids, are presently the most widely used constituents of non-viral gene carriers. Examined here is a particularly attractive cationic lipid class, triester phosphatidylcholines (PCs). These phospholipids are biodegradable, exhibit low toxicities and good transfection efficiency. A summary of studies on a set of over 30 cationic PCs revealed the existence of a strong, systematic dependence of their transfection efficiency on the lipid hydrocarbon chain structure. Transfection activity increases with increase of chain unsaturation from 0 to 2 double bonds per lipid and decreases with increase of chain length in the range ~28–50 total number of chain carbon atoms. Maximum transfection was observed for ethyl phosphate PCs (ePCs) with monounsaturated 14:1 chains (total of 2 double bonds and 28 carbon atoms in both chains). Because lipid phase behavior is known to depend strongly on the chain molecular structure, the described above quantitative structure-activity relationship (QSAR) substantiates a view that cationic PC phase propensities are an important determinant of their transfection efficiency. Indeed, X-ray structural studies showed that the rate of DNA release from lipoplexes as well as their transfection activity well correlate with non-lamellar phase progressions observed in cationic PC mixtures with membrane lipids. These findings appear to be of substantial interest because, according to current views, key processes in lipid-mediated transfection such as lipoplex disassembly and DNA release within the cells are believed to take place upon cationic lipid mixing with cellular lipids.

**Key words:** X-ray diffraction, gene therapy, non-viral vectors, cationic lipids
FABRICATION OF FUNCTIONALIZED MAGNETITE NANOPARTICLES WITH APPLICATIONS IN DRUG DELIVERY SYSTEMS

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\textsuperscript{1}“Horia Hulubei” National Institute for Physics and Nuclear Engineering, Magurele, Romania;
\textsuperscript{2}Politehnica University of Bucharest, Romania;

The use of nanotechnology in the fabrication of targeted carriers for anti-tumor substances is one solution for exceeding the tumor cells resistance to classical treatment schemes. We propose the obtaining of different drug delivery systems based on magnetite nanoparticles cores and organic shells to be used in the specific delivery of doxorubicin chemotherapeutic, in order to obtain specific toxic responses in human cancer cells.

The nanoparticles characterizing was done in terms of crystallinity, chemical composition and structure. Regarding the biological effects, the \textit{in vitro} cytotoxic potential was proved for different tumor models using both quantitative and qualitative estimations, correlated with the determinations of nanoparticles cellular entrapment efficiency using particle induced X-ray emission technique.

- **Key words:** magnetite nanoparticles, cancer, drug delivery systems;
ELECTROCHEMICAL APPROACH TO INVESTIGATE DRUG-NANOPARTICLES INTERACTIONS

M. Karabaliev, B. Tacheva

Trakia University, Faculty of Medicine, Stara Zagora, Bulgaria

Abstract

The interaction of three different drugs with Bovine serum albumin nanoparticles (BSA-NPs) is investigated in the work. Two phenothiazine drugs, chlorpromazine and thioridazine, and a spin-labeled chloroethylnitrosourea containing glycine (SLCNUgly) are used to explore the loading efficiency of BSA-NPs. The incorporation of the drugs in the BSA-NPs is investigated in situ by an electrochemical technique, a cyclic voltammetry (CV). Because all drugs are electroactive, by the aid of CV the concentration of the free nonincorporated drug can be determined in the solution. The presented results indicate penetration of the drugs in the BSA-NPs, according to their hydrophobicity.

Key words: Nanomedicine; BSA-NPs; albumine

1 Presenting author: miroslav.karabaliev@trakia-uni.bg
Introduction

Controlled drug delivery and release became an important issue in modern medication area during the last decades. The main goals are to reduce the drug dose rate and to prolong the release time in order to minimize poisonous side effects and to improve the therapeutic efficiency [1,2].

To achieve these goals suitable intelligent drug carriers are produced using different technological approaches. Micro- and nanoparticles and capsules with soft structure and tailorable properties have gained increasingly interest as vehicles for targeted drug delivery.

Albumin (bovine serum albumin (BSA) and human serum albumin (HSA)), is universally employed as a vehicle of molecular probe [3] and drug carrier [4, 5] for cancer diagnostics [6,7] and therapy, due to its excellent biocompatibility and biodegradability. The first commercial product based on albumin NPs in oncology is the 130 nm albumin-bound paclitaxel approved by the Food and Drug Administration (FDA) of USA in 2005 [8].

It was shown that albumin nanoparticles are suitable for encapsulation of hydrophobic drugs in solution [5]. In this work we used three drugs of amphiphilic and hydrophobic nature in order to test the incorporation ability of Bovine serum albumin nanoparticles (BSA-NPs). All drugs were electroactive, thus allowing the use of electrochemical methods of investigation [9].

Nitrosourea N-[(N’-(2-chloroethyl)-N’-nitrosocarbamoyl)-glycine amid of 2,2,6,6-tetramethyl-4-aminopiperidine-1-oxyl (SLCNUgly) is a spin labeled analogue of the clinically used non-labeled antitumor drug N’-cyclohexyl-N-(2-chloroethyl)-N-nitrosourea (lomustine, CCNU) (Figure 1).

It has been demonstrated in previous in vivo studies that SLCNUgly exhibited lower general toxicity comparing to that of CCNU [10, 11].

Two antipsychotic phenothiazine drugs, chlorpromazine and thioridazine, were used to investigate the loading efficiency of BSA-NPs toward drugs with amphiphilic nature.
Materials and Methods

Preparation of BSA-NPs
The preparation of BSA-nanoparticles was described earlier [12]. The method of preparation was as follows: BSA nanoparticles (NPs) were prepared by a desolvation technique. 200 mg BSA was dissolved in 2.0 mL Milli-Q water and the pH was adjusted to 7.4 with 0.01 M NaOH. Under constant stirring at 500 rpm, 8.0 mL ethanol was continuously added with a rate of 0.5 mL/min using a peristaltic pump. 200 µL of 8% glutaraldehyde solution was added gradually to crosslink the formed BSA particles during desolvation. After 24 h incubation at 20 °C under constant stirring, the NPs were purified by repeated centrifugation at 10000 rpm and re-dispersed in Milli-Q water under the assistance of ultrasonication. The BSA NPs were finally freeze-dried and stored at 4 °C before use.

Cyclic voltammetry
The interactions of the drugs with the BSA-NPs were tested by cyclic voltammetry (CV) because all three drugs are electroactive. Cyclic voltammetry is a convenient method for determination of the charge transfer between an electrode and electroactive drug in the solution. The measurements were made with potentiostat/galvanostat with FRA module.
VersaSTAT 3F (Princeton Applied Research). Three-electrode electrochemical cell was used in the work. The working electrode was Glassy carbon electrode with 3mm diameter. Ag/AgCl was used as reference electrode and the counter electrode was a Pt wire.

**Results and Discussion**

*Electrochemical characterization of the drug-BSA-NPs interactions*

The drug-NPs interactions were investigated *in situ* in the electrochemical cell. First, the drug was added to the electrochemical cell and the CV was taken. After that BSA-NPs were added into the cell, the solution was stirred with a magnetic stirrer, and another CV was taken. In Figure 2 are shown two voltammograms of SLCNUgly – taken before and after the addition of BSA-NPs in the solution.

The presented results suggest that the SLCNUgly drug is incorporated in the BSA-NPs after the NPs addition to the electrolyte solution. After the addition of BSA-NPs both the oxidation and reduction peaks decrease by value, most probably because of the incorporation of the drug in the core of the BSA-NPs.

Similar results were obtained for chlorpromazine and thioridazine. On Figure 3 are presented results for chlorpromazine. As can be seen, the decrease of the oxidation and reduction peaks was significant but somewhat smaller than the decrease for SLCNUgly.

![Figure 2. Cyclic voltammograms of SLCNUgly obtained without BSA-NPs (dashed red curve) and with 0.3 mg/mL BSA-NPs (solid blue curve); 0.4 mM SLCNUgly in 0.1 M KCl, 4 mM phosphate buffer (Na₂HPO₄–NaH₂PO₄), pH 7.4; scan rate 0.1 V/s; (reference electrode - Ag/AgCl)](image-url)
Figure 3. Cyclic voltammograms of chlorpromazine obtained without BSA-NPs (dashed red curve) and with 0.3 mg/mL BSA-NPs (solid blue curve); 0.4 mM chlorpromazine in 0.1 M KCl, 4 mM phosphate buffer (Na$_2$HPO$_4$–NaH$_2$PO$_4$), pH 7.4; scan rate 0.1 V/s; (reference electrode - Ag/AgCl)

Another possible explanation of the obtained results is a blocking of the electrode surface by the NPs themselves, thus hampering the charge transfer from the drug molecules in the solution. In order to check this assumption another electroactive specie was used. Potassium ferricyanide (K$_3$[Fe(CN)$_6$]) and potassium ferrocyanide (K$_4$[Fe(CN)$_6$]), as equimolar mixture, were used as electroactive species added to the electrolyte. This couple was chosen because it is highly hydrophilic, excluding thus hydrophobic interaction with the BSA-NPs. The results are shown in Figure 4.

Figure 4. Cyclic voltammograms of potassium ferri/ferrocyanide Fe(CN)$_{6}^{3+/4+}$ obtained without BSA-NPs (dashed curve) and with 0.3 mg/mL BSA-NPs (solid curve); 1 mM potassium ferri/ferrocyanide Fe(CN)$_{6}^{3+/4+}$ in 0.1 M KCl, 4 mM phosphate buffer (Na$_2$HPO$_4$ -NaH$_2$PO$_4$), pH 7.4; scan rate 0.1 V/s; (reference electrode - Ag/AgCl)
In contrast with the SLCNUgly, chlorpromazine and thioridazine drugs in the case of ferri/ferrocyanide a very little decrease of the redox peaks is observed (dashed and solid curve in Fig.4). This exclude the discussed possibility of electrode blocking from the BSA-NPs and supports the incorporation of chlorpromazine, thioridazine and SLCNUgly in the NPs core.

Concentration dependence of the drug-NPs interaction

The incorporation of the drugs into the BSA-NPs is investigated for different NPs concentrations. The results are shown in Fig. 5 as a relative decrease of the oxidation peak from its initial value.

All three drugs chlorpromazine, thioridazine and SLCNUgly exhibit significant decrease of the oxidation peak (curves 2, 3 and 4 in Fig.5). In contrast, the value of the oxidation peak of ferricyanide remain more than 90% from the initial value (curve 1 in Fig. 5).

In Figure 6 are compared the values of the “incorporation ability” of the BSA-NPs, according to the relative decrease of the oxidation peak of each drug. The relative decrease is derived as $(I_0 - I_2)/I_0 \times 100\%$, where $I_0$ is the oxidation peak value before the addition of BSA-NPs in the solution, and $I_2$ is the oxidation peak value after the addition of BSA-NPs with final concentration of 0.2 mg/ml in the solution.

![Figure 5. Dependence of the drugs oxidation peak current Ip on the BSA-NPs concentration. Curve 1 – 1 mM potassium ferri/ferrocyanide Fe(CN)$_6^{3-/4-}$; Curve 2 – 0.4 mM chlorpromazine; Curve 3 – 0.4 mM thioridazine; Curve 4 - 0.4 mM SLCNUgly. The results are presented as relative change of the peak value starting from the initial value before any addition of NPs in the solution. Electrochemical cell: 0.1 M KCl, 4 mM phosphate buffer (Na$_2$HPO$_4$ – NaH$_2$PO$_4$), pH 7.4; scan rate 0.1 V/s; reference electrode - Ag/AgCl.](image-url)
The results in Fig. 6 support the idea of the hydrophobic interaction of the drugs with the BSA-NPs. Thioridazine is known to be more hydrophobic than chlorpromazine [13] and SLCNUgly is even more hydrophobic, according to their ability to dissolve in water solution. According to the results in Fig. 6 thioridazine interacts 1.75 stronger than chlorpromazine. It is interesting to note that this value is similar to the partition coefficients ratios for the two drugs, reported in [13] – respectively 1.49 for erythrocytes and 2.22 for liposomes.

**Conclusions**

Using electrochemical technique, such as CV, the interactions of electroactive drugs and BSA-NPs are easily investigated. The incorporation of the drugs into the BSA-NPs is in the increasing order chlorpromazine, thioridazine, SLCNUgly. This order is in accordance with the hydrophilicity of the drugs, suggesting hydrophobic interaction between the drugs and the NPs.
References:


CG MOLECULAR DYNAMICS STUDY OF INDOLICIDIN IN WATER SOLUTION

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Antimicrobial peptides (AMPs) are small cationic membrane-active peptides with simple structure - from few to several tenth of amino acid residues. They are found in most living organisms and play an essential part in innate immunity. AMPs exhibit broad-spectrum antimicrobial activity against bacteria, fungi and viruses and can be potential candidates for alternative drugs.

The behavior of AMPs before interaction with the membrane and possible formation of clusters can influence significantly their activity. We investigated the behavior of three systems with different concentrations of antimicrobial peptide - Indolicidin in water solution, namely (10.9mM, 21.9mM and 99.4mM) by means of Coarse-Grained Molecular Dynamics simulations. This cationic antimicrobial agent is the shortest natural AMPs – only 13 amino acids with a largest proportion of tryptophan (Trp) residues of any known protein.

At 99.4mM, we observed saturated solution of Indolicidin. Under certain threshold concentration value (between 99.4mM and 21.9mM) globular amphipathic clusters are formed with average diameter of 4.5 nm. The form and the structure of these globular clusters are in agreement with experimental data published by [Hsu, C.. 2005]. These clusters are with a central hydrophobic core composed of proline and tryptophan, which is bracketed by positively charged regions near the peptide termini. This form of the cluster appears to be ideal for intercalation between the lipid molecules of a bacterial bilayer. Our results shed light on the behavior of the antimicrobial agent Indolicidin I solution and will be used in a virtual assessment of interaction between AMPs with bacterial membrane.

Citations:

- Key words: antimicrobial peptides, AMPs, indolicidin, molecular dynamics, coarse grained (CG);
VIPOXIN EFFECTS ON THE SURFACE ELECTRICAL PROPERTIES AND MEMBRANE TRANSPORT OF PROTONS IN HUMAN ERYTHROCYTES

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The main and most toxic component isolated from the venom of Bulgaria Vipera ammodites meridionalis is the neurotoxin Vipoxin - a heterodimeric postsynaptic ionic complex composed of two protein subunits – a basic and strongly toxic His48 sPLA2 (secretory phosphatide sn-2 acylhydrolase, Phospholipase A2, EC 3.1.1.4) enzyme (PLA2) and an acidic, enzymatically inactive and nontoxic component (VAC). Both subunits have the same polypeptide length (122 amino acids) and are closely related sharing 62\% sequence identity.

The effects of sPLA2, VAC and Vipoxin on the electrophoretic mobility (EPM), zeta potential ($\zeta$) and surface charge density on erythrocyte membranes were presented. EPM was measured by microscopic (visual) microelectrophoresis with an OPTON Cytopherometer (Austria). There was a strong enhancement in the negative charge on the erythrocyte membrane in the presence of VAC at concentration of 1.3 $\mu$M.

Extracellular proton concentration (H+ex) as a function of time (s), calculated from the recorded extracellular $\Delta$pH changes induced by sudden jumps of the extracellular proton concentration upon the treatment of erythrocytes by venom components, was measured by the modified method of Glaser (1984). VAC induced an increase in the slope of the curve and the maximum value of the proton concentration in extracellular space in erythrocytes in norm due to the lower pI of the acidic subunit - VAC. Vipoxin and its components altered the slope and maximal value of $\Delta$pH changes in erythrocytes in patients possessing lower value of $\zeta$ potential.

The correlation between the zeta potential and the effect of vipoxin potential shows that electrokinetic parameters could be used for the assay of toxic activity of different venom components.

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TRANSFORMATION OF PHENOMENOLOGICAL MODELS OF SODIUM-POTASSIUM PUMP INTO BIOPHYSICALLY BASED ONES

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Abstract

Production of action potential in any excitable cell is accompanied by ion movements along their concentration gradients across the membrane. To support the cell ready for a prolonged activity, the ions must be returned back against their gradients. The sodium-potassium pump is the main player in performing this task. It is widely studied both experimentally and mathematically. Mathematical model is not only a measure of our understanding of the processes but also a way to estimate the weight or importance of different parameters in the process. There are a few phenomenological models of sodium-potassium pump of different complexity that are used in models of activity of excitable structures, such as heart, muscle or nerve cells. They are relatively simple and characterize the steady state pump current through few affinities. The aim of the present study is to show a way for expansion the phenomenological models.

To obtain biophysically based model of sodium-potassium pump, the pump activity is represented by a cycle of chemical reactions between different pump states. That approach could give analytic expression for the steady state current, but require providing all the involved rate constants. By assuming sufficient number of states so that each transition reflects an elementary process, a linear dependence of rate constants on concentrations is expected according to the mass action law. This allows expression for the steady state pump current to be transformed from a function of rate constants into a function of concentrations. Then, the steady state pump current would depend on the available free energy and on a set of properly defined pump affinities. The general expression for the steady state pump current provides a way to estimate the quality of the phenomenological models and gives a framework for their expansion over much wider parameter set. To include dependence on the available free energy in phenomenological models, one needs no additional experimental information. Such models would predict correct direction of the current not only for forward but also for backward regime of the pump. Further refining of the phenomenological models would require information on the neglected affinities.

Key words: transporter; Na-K-ATPase; affinity; free energy
Introduction

Production of action potential in any excitable cell is accompanied by ion movements along their concentration gradients across the membrane. To support the cell ready for a prolonged activity, the ions must be returned back against their gradients. The Na+/K+ ATPase (NKA) is the main player in performing this task. It is widely studied both experimentally and mathematically.

In biophysically based models, the action of the pump is generally represented by a cycle of chemical reactions (for review see Glyn 1993; Glyn 2002). A system of differential equations corresponds to the transporters cycle. To study the NKA current one could use direct numerical integration of the set of differential equations corresponding to the transporter cycle. This approach has potential to describe quantitatively all the aspects of pump behaviour, if all the rate constants could be provided. Alternatively an exact analytic solution for the steady state current of a cycle could be obtained from the same set of differential equations (King and Altman 1956; Hill 1977; Hill 1989). The solution looks like rational function with two terms above and many terms below the line. Each of the terms below the line is the product of rate constants, which are mainly unknown. There are at least 30 rate constants for the NKA – 15 of them forward and 15 backward (Smith and Crampin, 2004). However, only some of them have been measured (Schulz & Apell, 1995; Schneeberger & Apell, 1999; Holmgren et al. 2000; De Weer et al., 2001, Gadsby et al., 2012). So both approaches adopt approximations to calculate the NKA current. In both cases the most common approximation is to reduce the number of states in the cycle to 2-6 (Hernandez et al., 1989, Gadsby and Nakao. 1989, Sagar and Rakowski 1994, Smith and Crampin, 2004; Oka et al., 2010; Garcia et al. 2012). This is accompanied with more complex expressions used to define individual rate constants (Smith and Crampin, 2004, Garcia et al. 2012, Lewalle et al. 2014). Such simplified models faced problems to reflect inter-tissue and inter-species differences (Lewalle et al. 2014). Attempts have been made to increase complexity of their 4-state NKA model (Garcia et al. 2012, Lewalle et al. 2014).

Alternative approach is to construct phenomenological model of the steady state current directly based on the experimental data for that current. Historically such approximations to the sodium pump current were defined by the authors of computer models. DiFrancesco and Noble, (1985) proposed eq. (1) for the sodium pump current in their model of cardiac myocytes. Latter Luo and Rudy (1994) modified it to include pump potential dependence as measured by Gadsby and Nakao (Gadsby and Nakao. 1989 Nakao and Gadsby. 1989) and obtained eq. (2).

\[
I_{pmp} = P_0 \frac{[K_o]}{[K_o]+pK_o} \frac{[Na_i]}{[Na_i]+pNa_i} \quad (1)
\]

\[
I_{pmp} = P_0 \frac{[K_o]}{[K_o]+pK_o} \frac{1}{1+ \frac{pNa_i}{[Na_i]+1.5} \frac{1}{1+0.1245e^{-0.197R_2}+0.0365e^{-pV} R_1}} \quad (2)
\]
Where $P_0$ is the maximal current, $\sigma = \frac{1}{7} (e^{\frac{[\text{Nao}]}{87.3}} - 1)$, $[\text{Ko}]$, $[\text{Nai}]$ and $[\text{Nao}]$ are external potassium, internal and external sodium concentrations, respectively; $pko$ and $pna$ are corresponding affinities; $V$ is membrane potential; $F$ and $R$ are the Faraday and universal gas constants, $T$ is absolute temperature.

Such models are wildly used and the Luo and Rudy model have become the standard model of choice for NKA (Wallinga, 1999; Pandit et al. 2001; Bondarenko et al. 2004; Hund & Rudy, 2004; Shannon et al. 2004; Ten Tusscher et al. 2004; Fortune and Lowery 2009; Grandi et al. 2010). Phenomenological equations like eq. (1, 2) are simple, easy to use and to calculate. Unfortunately they also have drawbacks. It is not clear when the approximation is no more valid. Neither how to modify the equation to expand the range of validity. The aim of the present study is to show a way for expansion the phenomenological models, on the basis of the set of differential equations that describe the pump.

**Method**

In the steady state conditions, when the time derivatives are zero the set of differential equations that describes transporters, is reduced to a system of algebraic equations (King and Altman, 1956; Hill, 1977). Following King and Altman (1956) and Hill (1977), one could write the exact analytic solution for the actual turning rate of the NKA – $Ist$. We would assume that the states of the transporter form a single cycle as then, the solution of the system has a more simple form. Such transporter has two modes of action – forward and backward ones. We would denote the rate constant for transition between states $i$ and $j$ in forward direction as $\alpha_{i,j}$ or $\alpha_i$ and in backward direction as $\beta_{i,j}$ or $\beta_i$. The general solution for an $n$-state cycle is direct expansion of the eq. 4 (Hill, 1977, Hill, 1989):

$$Ist = \frac{\alpha_{1,2}\alpha_{2,3}...\alpha_{n-1,n}\alpha_{n,1}\beta_{1,2}\beta_{2,3}...\beta_{n-1,n}\beta_{n,1}}{(\alpha_{2,3}...\alpha_{n-1,n}\alpha_{n,1}+\alpha_{3,4}...\alpha_{n,1}\beta_{1,2}+(n-2) \text{ other terms in a group})+(n-1) \text{ other groups}}$$

(3)

Note that $Ist$ as well as the rate constants have dimension of $s^{-1}$.

We would assume that sufficient number of transporter states is defined, so that each rate constant involved in binding/release of a substance would represent an elementary process. For those rate constants we will have linear dependence on concentrations:

$$\alpha_k = \alpha'_k[Sb_k] \quad \beta_i = \beta'_i[Sr_i]$$

(4)

where $\alpha'_k$ and $\beta'_i$ do not depend on concentrations; $[Sb_k]$ is the concentration of the $k$-th binding substance as defined for a forward process; $[Sr_i]$ is the concentration $l$-th released substance as defined for a forward process. This is in contrast to the models with reduced number of states, where the rate constants have to represent global estimates of the effects of a few transitions.
Terms above the line in eq. (3) have close relation with the thermodynamic force that drives the transporter (Hill, 1977, Hill, 1989). For rate constants that form a complete cycle one could write:

$$\frac{\alpha_1 \alpha_2 \alpha_3 \cdots \alpha_{n-1} \alpha_n}{\beta_1 \beta_2 \beta_3 \cdots \beta_{n-1} \beta_n} = \exp(Y / RT) = e^X$$

(5)

where Y is the total, associated with the transported substances free energy. Further for clarity we would redefine X=Y/RT and would name X as total driving force.

**Results**

To obtain steady state current for NKA (a transporter that couples outward movement of 3 sodium ions, inward movement of 2 potassium ions with a hydrolysis of ATP), we have to find the driving force. Following Smith and Crampin, (2004) we assume that ATP hydrolyses into ADP, P and H+. For NKA the total force looks like (Hill, 1977, Smith and Crampin, 2004):

$$X = \frac{dG_{atp}}{RT} + \ln \left( \frac{[ATP]}{[ADP][P][H]} \right) - 3 \ln \left( \frac{[Na_o]}{[Na_i]} \right) + 2 \ln \left( \frac{[K_a]}{[K_i]} \right) + (3z_{na} - 2z_k) \frac{F V}{RT}$$

(6)

Where [Na_o], [Na_i], [K_o], [K_i], represent concentrations of external and internal sodium and potassium. [ATP], [ADP], [P] and [H] represent concentrations of ATP, ADP, P and H+. \(dG_{atp}\) is a standard free energy of the ATP hydrolysis. V represents membrane potential, F, R, and T have their usual meaning. \(z_{na}=z_k=1\) is charge of sodium and potassium ions.

By dividing the upper and lower parts of the eq. (3) by \(\beta_1 \beta_2 \beta_3 \cdots \beta_{n-1} \beta_n\) and applying eq. (4) and eq. (5) one could obtain general expression for the steady state NKA actual turning rate:

$$\text{Ist} = \frac{e^{X-1}}{A e^{X+B}}$$

(7)

$$A = a_0 \left( 1 + \sum \frac{q_i (F - V_i)}{RT} \right) + \frac{P_{na_i}}{[Na_i]} + \frac{P_{ko}}{[Ko]} + \frac{P_{atp}}{[ATP]} + \frac{[Na_o]}{P_{na_o}} + \frac{[K_i]}{P_{ki}} + \frac{[P]}{P_p} + \frac{[H]}{P_h} + \frac{[ADP]}{P_{adp}}$$

$$B = b_0 \left( 1 + \sum \frac{q_i (F - V_i)}{RT} \right) + \frac{Q_{na_o}}{[Na_o]} + \frac{Q_{ki}}{[K_i]} + \frac{Q_{adp}}{[ADP]} + \frac{Q_p}{[P]} + \frac{Q_h}{[H]} + \frac{[Na_i]}{Q_{na_i}} + \frac{[K_o]}{Q_{ko}} + \frac{[ATP]}{Q_{atp}}$$

\(\sum\) indicates sum over the effects of the effective charges \(-q_i, q_i\). The affinities Pi, Qi could be functions of the concentrations and the potential, a0 and b0 characterize the pump maximal turning rare for the forward and backward process respectively. X is defined by eq. (6).

We would inspect the expressions for the NKA phenomenological models, to obtain impression how the affinities could look like. DiFrancesco and Noble, (1985) proposed eq. (1) for a model of NKA current (actual turning rate). One could write:
where we used that for forward moving of the pump eX>>1.

We see that as compared with eq. (7) the model for the sodium pump current proposed by DiFrancesco and Noble, (1985) is much simpler. To obtain it one has to neglect most of the affinities defined in eq. (7) except two. One of the affinities, we chose it to be $P_{\text{ae}} = pko$ is a constant, the other depends on concentrations $P_{\text{pV'}} = pnai \left(1 + \frac{[\text{Ko}]}{[\text{Na}]}\right)$, where $P_{\text{ko}}, P_{\text{nai}}$ are our affinities for the DiFrancesco and Noble model, pko, pnai are those of the DiFrancesco and Noble.

Similar expressions could be obtained also for the Luo and Rudy (1994) model of the sodium pump current. The model of Luo and Rudy (1994) is more complex than that of DiFrancesco and Noble, (1985), as it defines four affinities.

**Discussion**

Two distinct approaches succeed to describe the steady state NKA current. Biophysical models are characterized by the rate constants, while empirical ones by the affinities. The biophysically based models have clear origin, reflect both the static and dynamic properties of the NKA. However, the obtained results are complex and hard to interpret. Empirical models are valid only for the steady state current. They are simple and easy to use. However they have unclear origin and range of validity. For the case of the steady state current the link between both approaches is revealed.

The steady state current of the biophysically based models, obtained by numerical integration or analytically, is represented by the well-known eq. (3). To obtain the current, one needs information on all the rate constants that is often unavailable when the cycle is formed by significant number of states. We identified an alternative approach to deal with the eq. (3). Instead of decreasing the number of states and complicating the rate constants, we propose to do the opposite – to use all the states. Then the eq. (3) would be transformed into a rational function of concentrations, which would express the exact concentration dependence of the steady state current. By combining terms that have some certain concentration as a common factor, the terms in the rational function could be grouped to form the affinities. This allows evaluating the significance of the entire group instead of studying individual terms. So the complexity of the eq. (3) could be transformed into definitions of the individual affinities. That is a way to connect the empirical models with the biophysically based ones.
We obtained that the current would depend on affinities to both binding and released substances. Not only absence of binding substance could stop the transporter cycle, but also the excess of a released substance may cause transporter to be unable to continue. Both cases would cause the transporter to stop. That is in contrast to the rate constants in chemical reaction as well as reaction rate in the Michaelis – Menten equation that depend only on the binding substances.

Transition from the Michaelis – Menten affinities to the theoretical prediction as obtained in this paper (eq. 6, 7) is trivial, as is demonstrated by eq. (8). Thus empirical models could be regarded as approximations to the theoretical prediction. This allows when necessary, to expand the empirical models by theoretically defined affinities to any desired degree of accuracy. As the affinities could be measured experimentally, one can obtain approximations to the affinities as good as one could measure.

In skeletal muscles, NKA apparent affinity for internal sodium could be changed by hormones or by excitation (Buchanan et al. 2002; Shattock 2009; Clausen 2013). Hormones are not a part of NKA cycle. Therefore, one has to write separate cycles for normal and modified NKA. However, the same kinds of affinities would be defined in any transporter cycle version. According to our approach, differences in the transporter instances would be transformed into differences in the affinity values. Thus, the effect of hormones or excitation could reflect a possible ligand or voltage gated transitions between different modifications of the pump that could induce changes in affinity observed in experiments.

**Conclusions**

In this paper the well known analytic solution for the steady state NKA current was studied. It was rearranged to reflect the affinities defined by phenomenological models. So obtained model – eq. (6, 7) on one hand have clear biophysical origin, on the other like in the phenomenological models the current is simple as it is fully characterized by its affinities. Thus proposed model combines best features of the biophysically based models and the phenomenological ones.
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MODIFICATION WITH SHORT LASER PULSES OF COLLAGEN DERIVED MATRICES CROSSLINKED WITH D-FRUCTOSE FOR POTENTIAL USE IN THE REGENERATIVE MEDICINE

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New biomaterials with improved functionality, biocompatibility and low immunogenicity are a major focus of research in the regenerative medicine and the related interdisciplinary fields. The collagen family proteins comprise the largest percentage of the total protein mass in the body therefore they are among the first choices as compound of such biomaterials. Unfortunately the collagen processing increases its solubility and decreases its mechanical strength. To overcome these issues often crosslinking is applied. However many crosslinking agents impact negatively the toxicity and immunogenicity of the biomaterial. Therefore as a prerequisite of better biocompatibility the biomaterials studied here are made of naturally occurring compounds. Further the appropriate biomaterial texture and patterning emerges in the recent years as important aspect of the successful cell compatibility and regeneration and lasers offer the advantage of high precision and minimization of chemical contaminations in such biomaterial processing.

Purpose of the study is to evaluate the laser surface modification and micropatterning of newly synthesized collagen-derived crosslinked biomaterials for potential use in the regenerative medicine.

Methods: The matrices were casted in the form of thin films with smooth surface and prepared from collagen derived from tendon and crosslinked with D-fructose in custom crosslinker. Quantronix Integra C ultrafast laser system was used to generate the short laser pulses with 790nm center wavelength and different varied parameters sets (such as duration and number of pulses, fluence, etc.) which were applied on the samples. The resulted surface modifications were examined with optical and SEM microscopy.

Results: In surface modifications with regimes and parameters of the beam where photomechanical effects were achieved the shape of the resulting cavities and degree of foaming is influenced by the level of the crosslinking agent in the matrix, in regimes of operation above the threshold of plasma formation such relation is less pronounced. The systematic exploration in the study of the relations between the parameters of the laser beam, the matrix composition and the resulted surface modifications and microstructures give us more control in producing biomaterial with specific surface microgeometry favoured by particular cell line or tissue that needs to be regenerated.

Key words: 1,3,4,5,6-Pentahydroxy-2-hexanone, ablation, biocompatibility, scaffold, surface patterning, tissue engineering.
Session
Radiology and Roentgenology 3
RADIATION EXPOSURE OF PATIENTS FROM TWO PROCEDURES
ON NEW SPECT-CT SYSTEM

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Abstract

After the first national survey of patient exposures from hybrid imaging in nuclear medicine was performed in Bulgaria, a new single-photon emission computed tomography and computed tomography (SPECT-CT) system was installed. The purpose of this study is to estimate patient doses received from procedures on this system and to supplement data from the national survey.

The study was performed on a system GE Discovery NM/CT 670 Pro. Patient data were retrospectively collected from the picture archiving and communication system (PACS) of the hospital. Since this is a new hospital, enough statistics was available only for two types of examinations – bone imaging and myocardial perfusion, the latter including stress or stress and rest examination. Also it was performed with two different radiopharmaceuticals. Separate calculations for myocardial perfusion were made based on both criteria. Data were collected for 40 patients for the first and 42 patients for the second procedure. The methods for calculation of effective dose were the same as in the national survey for consistency, with some minor changes. The CT contribution to the dose was estimated with CT Expo software, applying the International Commission on Radiological Protection (ICRP) Publication 103 tissue weighting factors. The radiopharmaceutical contribution was estimated by multiplying the ICRP 53/80/106 corresponding conversion coefficients by the averaged on the whole patients’ sample administered activity.

For bone imaging the mean effective dose was 4.5 mSv from CT and 3.4 mSv from the radiopharmaceutical, hence the total effective dose was 7.9 mSv. For myocardial perfusion the CT contribution was 0.2 mSv for only stress, doubled for stress and rest. The 99mTc-tetrofosmin contribution to stress examination was 3.1 mSv and to stress and rest it was 7.2 mSv. The contribution of 99mTc-MIBI to the stress exam was 3.2 mSv and to the stress and rest exam the value was 8.7 mSv. The total weighted effective dose for myocardial perfusion was 4.6 mSv.

Doses from bone imaging are approximately in the middle of the range from the national survey. Doses from myocardial perfusion from the CT scanner are much lower compared to the other systems in the country and the exposure from the radiopharmaceutical is similar to them. Potential was found for optimization of bone imaging.
Introduction

The first single-photon emission computed tomography and computed tomography (SPECT-CT) systems started operating in Bulgaria in 2009. Examinations with these systems deliver relatively high radiation exposures to patients because two methods, using ionizing radiation, are combined: CT, exposing patients with X-rays, and SPECT, based on the use of gamma radiation emitting radiopharmaceuticals, introduced into patient’s body. First national survey of patient exposures from hybrid imaging in nuclear medicine was performed in 2013-2014, and diagnostic reference levels were elaborated [1, 2]. At that time four SPECT-CT systems were functioning in the country, and data from examinations performed on all of them were included in the study. In 2015 new SPECT-CT system was installed in a new hospital and it began operation in beginning of 2016. The purpose of this study is to estimate patient doses received from frequent procedures on this system and to supplement data from the national survey.

Materials and Methods

The SPECT-CT system is Discovery NM/CT 670 Pro (GE Healthcare), one of the latest products of this manufacturer. It includes 16-detector row CT, and the Adaptive Statistical Iterative Reconstruction (ASiR) algorithm, providing the opportunity to use low dose techniques for the CT examination, especially when CT is used only for attenuation correction and anatomical localization of activity distribution. Patient data were retrospectively collected from the picture archiving and communication system (PACS) of the hospital. Data included patient sex, age, weight, height, type of radiopharmaceutical (RPh) and administered activity, exposure data from the CT (tube voltage, rotation time, noise index when tube current modulation was used, pitch, collimated beam thickness, volume computed tomography dose index (CTD\textsubscript{vol}), and dose length product (DLP)).

Since this is a new hospital, enough statistics was available only for two types of examinations – bone imaging and myocardial perfusion, the latter including stress or stress and rest examination. Bone imaging was performed with $^{99m}$Tc-MDP, while myocardial perfusion was performed with two different radiopharmaceuticals – $^{99m}$Tc-MIBI and $^{99m}$Tc-Tetrofosmin.

The methods for calculation of effective dose were the same as in the national survey for consistency, with some minor changes. The CT contribution to the dose was estimated with CT Expo software (version 2.1, Medizinische Hochschule, Hannover, Germany), applying the International Commission on Radiological Protection (ICRP) Publication 103 tissue weighting factors [3]. This software provides the opportunity to select the examined part of the patient’s body with the CT scanner on standard mathematical male and female phantoms [4]. For the purpose of effective dose calculation the CT scanner model and averaged exposure parameters were introduced in the software. Bone imaging is in general a whole body examination, but different anatomic regions of the body were scanned depending on physician’s requirement. Patient data were separated by sex and anatomical region, and averaged CTD\textsubscript{vol} and DLP according to both criteria were entered in CT Expo. For myocardial perfusion standard region was always scanned and data were separated only by sex. The mean effective dose from CT contribution for bone imaging was calculated by
weighting by the number of patients depending on the anatomical region examined, averaged over both sexes. This is the only difference in the method used in comparison to the national survey, where the number of patients in every subgroup depending on the anatomical region was almost equal and such weighting wasn’t applied. In the case of myocardial perfusion, the effective dose of patients, receiving only stress, was doubled for those, receiving stress and rest examination, since the same CT protocol and scanned region was used.

The RPh contribution to patient exposure was calculated by multiplying the ICRP Publications 53/80/106 corresponding conversion coefficients by the averaged on the whole patients’ sample administered activity [5-7]. These coefficients are based on ICRP Publication 60 tissue weighting factors for calculation of effective dose [8]. In the case of myocardial perfusion separate calculations were performed for $^{99m}$Tc-MIBI and $^{99m}$Tc-Tetrofosmin, and also for patients receiving only stress, or stress and rest exam. Calculation of effective dose from the radiopharmaceutical was also performed using recently published by Andersson et al. conversion coefficients [9], based on the new ICRP/International Commission on Radiation Units and Measurements (ICRU) reference computational phantoms [10], ICRP Publication 107 decay data [11], and ICRP Publication 103 tissue weighting factors [3]. The authors of this study provide both separate and common conversion coefficients over both sexes. We used the common coefficients for simplicity. All conversion coefficients, used in this study, are presented in Table 1.

Table 1. Conversion coefficients for calculation of effective dose from administered activity in the present study.

<table>
<thead>
<tr>
<th>Radiopharmaceutical</th>
<th>Conversion coefficient (mSv/MBq)</th>
<th>ICRP 53/80/106</th>
<th>Andersson 2014</th>
</tr>
</thead>
<tbody>
<tr>
<td>$^{99m}$Tc-MDP</td>
<td></td>
<td>0.0057$^a$</td>
<td>0.00431</td>
</tr>
<tr>
<td>$^{99m}$Tc-Tetrofosmin stress</td>
<td></td>
<td>0.0069$^b$</td>
<td>0.00576</td>
</tr>
<tr>
<td>$^{99m}$Tc-Tetrofosmin rest</td>
<td></td>
<td>0.0080$^c$</td>
<td>0.00629</td>
</tr>
<tr>
<td>$^{99m}$Tc-MIBI stress</td>
<td></td>
<td>0.0079$^a$</td>
<td>0.00655</td>
</tr>
<tr>
<td>$^{99m}$Tc-MIBI rest</td>
<td></td>
<td>0.0090$^a$</td>
<td>0.00703</td>
</tr>
</tbody>
</table>

$^a$ICRP Publication 80 (1998)
$^b$ICRP Publication 106 (2008)
$^c$4th Addendum to ICRP Publication 53 (2014)
Results

Estimations of effective dose $E$ were performed for a group of 40 patients undergoing bone imaging (21 males and 19 females), 19 patients receiving myocardial perfusion with $^{99m}$Tc-MIBI, and 23 patients receiving myocardial perfusion with $^{99m}$Tc-Tetrofosmin (total of 35 males and 7 females). Also 32 of the patients, that underwent myocardial perfusion, had only stress, while the other 10 patients had stress and rest exam. Usually a one-day protocol was used on them. Table 2 presents the mean values, standard deviation (SD), minimum and maximum of administered activities, CTDI$_{vol}$ and DLP for both types of examinations. The calculated effective dose $E$ per examination is shown in Figure 1. The first columns for each exam on the graph represent the CT contribution to $E$, the second columns describe $E$ from the SPECT component, applying ICRP 53/80/106 conversion coefficients, the third columns describe $E$ from the SPECT component, applying Andersson’s coefficients [9], and the fourth columns show the total $E$, taking into account the radiopharmaceutical contribution, calculated with ICRP 53/80/106, for consistency with the national survey.

Table 2. Type of examination and radiopharmaceutical, and corresponding mean values, standard deviation (SD), minimum and maximum of administered activities, CTDI$_{vol}$ and DLP.

<table>
<thead>
<tr>
<th>Type of examination</th>
<th>Radiopharmaceutical</th>
<th>A (MBq)</th>
<th>CTDI$_{vol}$ (mGy)</th>
<th>DLP (mGy cm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bone imaging</td>
<td>$^{99m}$Tc-MDP</td>
<td>605 ± 111</td>
<td>3.8 ± 1.2</td>
<td>243 ± 100</td>
</tr>
<tr>
<td></td>
<td>Min - Max</td>
<td>444 - 740</td>
<td>1.6 - 6.4</td>
<td>63 - 400</td>
</tr>
<tr>
<td>Myocardial perfusion stress</td>
<td>$^{99m}$Tc-Tetrofosmin</td>
<td>439 ± 78</td>
<td>0.8 ± 0</td>
<td>14 ± 1</td>
</tr>
<tr>
<td></td>
<td>Min - Max</td>
<td>370 - 555</td>
<td>0.8 - 0.8</td>
<td>12 - 17</td>
</tr>
<tr>
<td>Myocardial perfusion rest</td>
<td>$^{99m}$Tc-MIBI</td>
<td>403 ± 51</td>
<td>0.8 ± 0</td>
<td>14 ± 1</td>
</tr>
<tr>
<td></td>
<td>Min - Max</td>
<td>370 - 555</td>
<td>0.8 - 0.8</td>
<td>12 - 17</td>
</tr>
<tr>
<td></td>
<td>$^{99m}$Tc-Tetrofosmin</td>
<td>601 ± 93</td>
<td>0.8 ± 0</td>
<td>14 ± 1</td>
</tr>
<tr>
<td></td>
<td>Min - Max</td>
<td>555 - 740</td>
<td>0.8 - 0.8</td>
<td>12 - 17</td>
</tr>
<tr>
<td></td>
<td>$^{99m}$Tc-MIBI</td>
<td>611 ± 77</td>
<td>0.8 ± 0</td>
<td>14 ± 1</td>
</tr>
<tr>
<td></td>
<td>Min - Max</td>
<td>555 - 740</td>
<td>0.8 - 0.8</td>
<td>12 - 17</td>
</tr>
</tbody>
</table>

Bone imaging

The mean age of patients, undergoing bone imaging was 61 years, and the mean weight was 73.3 ± 16.8 kg (mean ± standard deviation). The scanning parameters of the CT protocol were 120 kV tube voltage, 0.5 s rotation time, 20 mm (16 x 1.25 mm) collimated beam width, tube current modulation (TCM) with noise index 22, pitch 1.375:1.

The CT contribution to $E$ was 4.5 mSv (Figure 1). CT doses from bone imaging for all SPECT-CT systems from the national survey were 1.2, 1.8 and 7.2 mSv respectively [1, 2]. The third dose was reported to be from a diagnostic CT, which explains the high value. Our result is lower in comparison to the third one, but higher than the first two values. Comparison of mean CTDI$_{vol}$ reveals again, that the result from the present study, 3.8 mGy (Table 2), is higher than the result from the first two systems (1.7 and 2.3 mGy), and lower
than CTDI\textsubscript{vol} from the third system of 13.1 mGy. The SPECT-CT system in the present study is very similar (next version) to the third system, reported in the national survey. This result shows that significantly smaller exposure may be achieved by the proper setting of CT scanning protocols and justification of the use of diagnostic CT. However taking into account the lower CTDI\textsubscript{vol} and \( E \) values for the other two systems, some optimization of the protocol used presently may be searched. Moreover the diagnostic reference level (DRL) for CTDI\textsubscript{vol} was set to be 3 mGy [1, 2]. Also discussion was made with the nuclear medicine specialists concerning the length of the body region scanned, which was found longer compared to the others. The first survey reported scanning of chest or pelvis, chest or abdomen, or chest, with mean DLP values of 88, 99 and 523 mGy cm, for the three systems respectively. The DRL was set at 200 mGy cm. In the present case we had: neck, chest, abdomen and pelvis; or chest, abdomen and pelvis; or abdomen and pelvis, with mean DLP 243 mGy cm. This hospital is a specialized oncological center and mainly patients with oncological diseases are subject to bone imaging. Consecutively the whole body scanning is necessary for the correct diagnosis and follow-up of the disease and explains to some degree the higher value of \( E \) from the CT component.

![Figure 1](image.png)

**Figure 1.** Effective doses from bone imaging and myocardial perfusion, stress or stress and rest, the latter performed with \(^{99m}\text{Tc-Tetrofosmin}\) or \(^{99m}\text{Tc-MIBI}\). The first column for each exam represent the CT contribution to effective dose in millisievert, the second column describes effective dose from the SPECT component, applying ICRP 53/80/106 conversion coefficients, the third column describes effective dose from the SPECT component, applying Andersson’s coefficients [9], and the fourth column shows effective dose from the whole examination, taking into account the radiopharmaceutical contribution, calculated with ICRP 53/80/106.
The RPh contribution to $E$ using the old conversion coefficients was 3.4 mSv. Data from the previous study were 2.5, 3.4 and 2.9 mSv respectively. Analysis of the data collected showed different preferences of the physicians for the activities to be applied without any systematic reason (from 444 to 740, mean 605 MBq, Table 2). After discussions with the nuclear medicine specialists it was decided to apply 481-518 MBq to patients with standard sizes. Very few data are still available after this change and the impact on image quality is not clear yet. Further study should be performed to estimate the relevance of this decision. Applying the new conversion coefficients, $E$ was estimated to be 2.6 mSv, about 24% lower compared to the result with the old ICRP coefficients [9]. This result is expected because more realistic voxel phantoms, based on CT images of real humans, are the basis for derivation of the coefficients [10]. The same value is reported by Mattsson et al. for this exam [12]. New conversion coefficients are provided by ICRP for bone imaging [13]. They are based on ICRP Publication 60 tissue weighting factors, like ICRP 53/80/106. It is expected that they will also be replaced in a new publication that will be based on Andersson’s coefficients. That is why it was decided to use the previously published coefficients for comparison purposes with the data from the national survey.

Recent survey in the United States, published December 2015, reported average activity of $^{99m}$Tc-MDP, bone SPECT, across 225 facilities to be 930 ± 118 MBq, with a range of 710-1,315 MBq [14]. Information is not provided on gamma cameras age and models, covered by this survey. In 2014 a document of the European commission Radiation Protection No 180 “Medical Radiation Exposure of the European Population”, prepared under the Dose DataMed II project, in which Bulgaria also participated, was issued [15]. It reports mean activities for bone examinations from across Europe (data from 35 countries) from 518 MBq (Sweden) to 771 MBq (Spain), mean value for Europe of 662 MBq. Bulgarian data provided for the project state 605 MBq. The activities reported in Bulgaria from all 11 nuclear medicine centers, performing bone SPECT in 2014, vary between 555 and 740 MBq, with mean 647 MBq [16]. Doses from this examination are not high in our country, especially compared to the USA practice. However there are more possibilities to further reduce the doses by using the opportunities provided by the new equipment: higher sensitivity of the detectors and better calculation algorithms.

**Myocardial perfusion**

The mean age and weight of patients examined for myocardial perfusion were 59.3 years and 88.4 ± 14.4 kg respectively. The CT scanning data were 120 kV, 0.6 s rotation time, 20 mm (16 x 1.25 mm) collimated beam width, fixed tube current 20 mA, pitch 1.375:1.

The CT contribution to $E$ was 0.2 mSv for stress and 0.4 mSv for stress and rest examination (Figure 1). Data from the national survey are available for two systems and are 0.8 mSv for the system, performing stress and rest, and 1.3 mSv for the system, performing only stress [1, 2]. DRLs were chosen to be 3 mGy for CTDI$_{vol}$ and 70 mGy cm for DLP, while the present mean values for these parameters were 0.8 mGy and 14 mGy cm. The doses from the present study are quite low.

Effective doses from the RPh, ICRP 53/80/106 coefficients applied, were 3.2 mSv from stress examinations with both $^{99m}$Tc-Tetrofosmin and $^{99m}$Tc-MIBI, 7.2 mSv from stress and rest with $^{99m}$Tc-Tetsofosmin, and 8.7 mSv from stress and rest with $^{99m}$Tc-MIBI (Figure 1). These data using Andersson’s coefficients were as follows: 2.6, 2.6, 5.8 and 6.9 mSv. For this examination again $E$ with the new coefficients have lower values of the order of 19-21%. The administered activity doesn’t depend on the type of RPh (Tetrofosmin or MIBI based). Since the conversion coefficients have lower values for Tetrofosmin than for MIBI,
it was recommended to use Tetrofosmin for dose saving purpose. The stress and rest exams are 24% of the total number of myocardial perfusion examinations.

The International Atomic Energy Agency (IAEA) performed a very big international study in 2012-2013, focused on nuclear myocardial perfusion imaging – IAEA Nuclear Cardiology Protocols Cross-Sectional Study (INCAPS) [17]. Data were collected on 7911 patients in 308 departments in 65 countries. Mean $E$ reported was 10.0 ± 4.5 mSv. Variations between continents were from 7.9 ± 3.5 mSv (lowest value) for Europe, to 11.8± 4.1 mSv (highest value) for Latin America. Eight “best practices” were defined, among them: avoid too much technetium (highest recommended activity 1332 MBq and mean total $E < 15$ mSv); perform stress only imaging (if stress images are normal, the rest imaging can be avoided without compromising the quality of the diagnosis [18]; use camera-based dose-reduction strategies (CT attenuation correction, high-technology software and hardware); weight-based dosing for technetium. Lower doses were found among patients, examined in departments, adhering to more of the best practices. All best practices were recognized in our study. A substudy of the IAEA reported mean $E$ from SPECT in Europe 8 ± 3.4 mSv, with variations between the four regions: 8.2 ± 4.1 mSv for East, 6.9 ± 3.6 mSv for North, 8.3 ± 2.9 mSv for South, and 8.7 ± 3.7 mSv for West Europe [19]. Another substudy reported mean $E$ in the Oceania region 9.3 ± 3.7 mSv [20]. Radiation Protection No 180 publication determined mean $E$ in the European countries 3.8 mSv from stress with $^{99m}$Tc-Tetrofosmin, 4.8 mSv from stress with $^{99m}$Tc-MIBI, 4.1 mSv only from rest with $^{99m}$Tc-Tetrofosmin and 5.5 mSv only from rest with $^{99m}$Tc-MIBI [15]. Data from the Bulgarian national survey for SPECT contribution are 6.8 mSv from stress and rest exam on one of the systems and 3.9 mSv from stress on the second system, both performed with Tetrofosmin [1, 2].

In the present study total $E$, weighted over stress, and stress and rest exam, and also averaged over the types of RPh, taking into account CT contribution, was 4.7 mSv. The total $E$ from both systems included in the national survey was 7.6 mSv and 5.2 mSv. The myocardial perfusion practice in our nuclear medicine department is in step with the best practices in the world, which is proven by the low doses received from patients, comparable with the lowest reported doses at European and worldwide level.

Conclusions

Study of patient exposures from bone imaging and myocardial perfusion on a newly installed SPECT-CT system in Bulgaria was performed. It supplemented the data from the first national survey in hybrid imaging in nuclear medicine, performed in the country. Some potential for optimization of the CT protocol for bone imaging was found, and some decrease of administered activities of the radiopharmaceutical was proposed. The best practices of myocardial perfusion imaging are applied in the department and the doses from this examination are very low at international level. Effective doses from the administration of the radiopharmaceuticals, used in this study, calculated with the widely used ICRP conversion coefficients, are overestimated. The new coefficients, proposed by Anderson et al. [9], should be used in future studies to provide more precise information corresponding to the new dosimetry methods.
References:


16. National Centre of Radiobiology and Radiation Protection. Data from national surveys performed yearly.


RADIATION EXPOSURE OF PATIENTS FROM WHOLE BODY EXAMINATIONS ON NEW PET-CT SYSTEM

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University Hospital City Clinic, Sofia, Bulgaria

Abstract

First national survey of patient doses from hybrid imaging in nuclear medicine in Bulgaria was performed in 2013-2014. Afterwards new equipment was installed in the country. The purpose of this study is to supplement the information from the national survey by estimating radiation exposure of patients from the new positron emission tomography-computed tomography (PET-CT) system functioning in Bulgaria.

The system is GE Discovery IQ Clarity 5 ring. Patient data from whole body examinations with 18F-2-fluoro-2-deoxy-D-glucose (FDG) for 105 patients were retrospectively collected from the picture archiving and communication system (PACS) of the hospital. Same methods for calculation of effective dose from the PET and CT parts of the examination as in the national survey were used for consistency. The radiopharmaceutical contribution to patient exposure was determined by multiplying the averaged over all patients activity applied and the International Commission on Radiological Protection (ICRP) Publication 80/106 conversion coefficients. For the CT contribution CT Expo software was used.

The mean effective dose from the PET part of the examination for the whole cohort of patients was 4.4 mSv, 25% and 10% lower in comparison to the other two systems functioning in the country. The mean effective dose from the CT part was 3.6 mSv, applying the ICRP 103 tissue weighting factors, for the standard whole body examination. This value is about 53% lower than CT exposures calculated for the other two systems. Taking into account the overall exposure from the hybrid imaging, the mean effective dose was 8 mSv.

Patient doses from the new PET-CT system are up to 36% lower compared to the other systems in Bulgaria. Potential for further optimization is the use of iterative reconstruction algorithm of the CT scanner, expected to be introduced soon.

1 Presenting author: simona.avramova@cityclinic.bg
Introduction

Hybrid positron emission tomography-computed tomography (PET-CT) is a new method in nuclear medicine imaging that proved its important place in tumour, cardiology, neurology imaging and other applications [1, 2]. Although it has big diagnostic potential, this method is related to high levels of exposure and patient doses are of concern. During PET-CT imaging positron emitting radiopharmaceuticals (RPh) are introduced in patient’s body and annihilation radiation from positrons, with energy of 511 keV, is registered by the PET scanner. The system is combined with a CT scanner, emitting X-rays, usually used for attenuation correction and anatomical localization purposes. Both methods are using ionizing radiation and each of them is a high dose method. For this reason PET-CT imaging is one of the highest dose methods used for diagnostic purposes [3]. During 2013-2014 first national survey of patient exposures from hybrid imaging in nuclear medicine was performed in Bulgaria [4, 5]. It included information from both PET-CT systems, functioning in the country at that time. In beginning of 2016 new system began operation in a new oncological hospital. The purpose of this study is to supplement the information from the national survey by estimating radiation exposure of patients from the new PET-CT system, functioning in Bulgaria.

Materials and Methods

The PET-CT system is Discovery IQ Clarity 5 ring (GE Healthcare). This is one of the newest products of this manufacturer. It includes more sensitive detectors for PET detection and iterative reconstruction algorithms, providing the opportunity to administer lower activities of the RPh. Patient data were retrospectively collected from the picture archiving and communication system (PACS) of the hospital. The data collected were patient age, sex, weight, height, administered activity of the RPh, and CT scanning data: tube voltage, noise index of the tube current modulation system, rotation time, pitch, collimated beam thickness, volume computed tomography dose index (CTDlvol), and dose length product (DLP). Same methods for calculation of effective dose from the PET and CT parts of the examination as in the national survey were used for consistency. The RPh contribution to patient effective dose was determined by multiplying the administered activity, averaged over the patient’s sample, and the International Commission on Radiological Protection (ICRP) Publication 80 conversion coefficients [6]. The conversion coefficients are provided for ICRP Publication 60 tissue weighting factors [7]. The same values of the coefficients for the RPh used (18F-2-fluoro-2-deoxy-D-glucose (FDG)) are published in the newer publications ICRP 106 and ICRP 128 [8, 9]. Andersson et al. [10] published recently new conversion coefficients, based on more realistic voxel phantoms [11], new decay data [12], and ICRP Publication 103 tissue weighting factors [13]. Estimation of effective dose based on these new coefficients was also performed. The CT contribution was calculated with CT Expo software (version 2.1, Medizinische Hochschule, Hannover, Germany). The software provides the possibility to select the body regions scanned and to calculate effective doses separately for males and females. CT scanner model, exposure parameters, and averaged over all patient’s sample CTDlvol and DLP, separated by sex, were introduced in the software. The total CT contribution to patient effective dose was determined by averaging over both sexes. ICRP Publication 103 tissue weighting factors were selected as option in the software for consistency with the national survey data [13].
Results

Patient data were collected for 134 patients, undergoing PET-CT tumour imaging. All patients were examined with the radiopharmaceutical $^{18}$F-FDG. Two types of examinations were identified – the most frequent examination included patient scanning from head till mid thighs, named here “standard examination”, as in the national survey, although this is in fact a whole body exam [4, 5]. The second examination was rarely performed to patients with melanoma malignum, and it included scanning from head till feet. It is named “whole body examination” in this text, as in the national survey. Patients undergoing standard exam were separated by weight in two groups. The first group was selected to have body weight between 50 and 90 kg, as recommended in the literature for estimation of typical patient doses from diagnostic procedures, because enough statistics was available for that purpose [14, 15, 16]. The second group included all patients (all weights). The same approach to include all weights was used in the national survey. Patient statistics for the 50-90 kg group are summarized in Table 1. The same data for the second all weights group, are included in Table 2. Mean values, standard deviation (SD), minimum and maximum values of patient’s age, weight, administered activities, CTDI$_{vol}$ and DLP, separated by sex and type of examination, are included in the tables. Standard examination was performed on 91 patients in the first group, 31 males and 60 females. The second group included data on 48 males and 72 females for this exam. For whole body examination all patient data were included irrespective of patient’s weight, a total of 9 males and 5 females.

Table 1. Statistical data for patients, undergoing PET-CT tumour imaging with $^{18}$F-FDG, group of 50-90 kg body weight: mean values ± standard deviation (SD), minimum and maximum values of patient’s age, weight, administered activity, CTDI$_{vol}$ and DLP.

<table>
<thead>
<tr>
<th>Examination</th>
<th>Age (years)</th>
<th>Weight (kg)</th>
<th>A (MBq)</th>
<th>CTDI$_{vol}$ (mGy)</th>
<th>DLP (mGy cm)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Standard - 31 males</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean ± SD</td>
<td>61.3 ± 11.7</td>
<td>72.1 ± 10.7</td>
<td>242 ± 37</td>
<td>2.6 ± 0.9</td>
<td>280 ± 109</td>
</tr>
<tr>
<td>Min - Max</td>
<td>26 - 80</td>
<td>50 - 90</td>
<td>168 - 301</td>
<td>1.3 - 4.6</td>
<td>137 - 533</td>
</tr>
<tr>
<td><strong>Standard - 60 females</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean ± SD</td>
<td>55.6 ± 12.5</td>
<td>67.6 ± 9.7</td>
<td>225 ± 32</td>
<td>2.3 ± 0.9</td>
<td>252 ± 97</td>
</tr>
<tr>
<td>Min - Max</td>
<td>24 - 81</td>
<td>52 - 89</td>
<td>170 - 297</td>
<td>1.3 - 4.7</td>
<td>138 - 499</td>
</tr>
</tbody>
</table>

The scanning parameters of the CT were the same for both exams, with small difference in noise index of tube current modulation: 120 kV tube voltage, 0.6 s rotation time, 20 mm (16 x 1.25 mm) collimated beam width, tube current modulation (TCM) with noise index 28.8 (standard exam) or 28.5 (whole body exam), pitch 1.375:1. The calculated effective doses $E$ for the 50-90 kg group (standard exam) and for all patients receiving whole body exam, are presented in Figure 1.
Table 2. Statistical data for patients, undergoing PET-CT tumour imaging with $^{18}$F-FDG, all weights: mean values ± standard deviation (SD), minimum and maximum values of patient’s age, weight, administered activity, CTDI$_{vol}$ and DLP.

<table>
<thead>
<tr>
<th>Examination</th>
<th>Age</th>
<th>Weight (kg)</th>
<th>A (MBq)</th>
<th>CTDI$_{vol}$ (mGy)</th>
<th>DLP (mGy cm)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Standard - 48 males</strong></td>
<td></td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean ± SD</td>
<td>59.0 ± 12.7</td>
<td>83.8 ± 23.7</td>
<td>276 ± 74</td>
<td>3.2 ± 1.5</td>
<td>351 ± 168</td>
</tr>
<tr>
<td>Min - Max</td>
<td>26 - 81</td>
<td>50 - 145</td>
<td>168 - 464</td>
<td>1.3 - 6.7</td>
<td>137 - 719</td>
</tr>
<tr>
<td><strong>Standard - 72 females</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean ± SD</td>
<td>54.9 ± 12.2</td>
<td>69.2 ± 14.5</td>
<td>229 ± 47</td>
<td>2.5 ± 1.3</td>
<td>271 ± 136</td>
</tr>
<tr>
<td>Min - Max</td>
<td>24 - 81</td>
<td>36 - 108</td>
<td>123 - 358</td>
<td>1.2 - 6.1</td>
<td>125 - 651</td>
</tr>
<tr>
<td><strong>Whole body - 9 males</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean ± SD</td>
<td>45.9 ± 17.0</td>
<td>88.7 ± 18.7</td>
<td>308 ± 60</td>
<td>3.5 ± 0.8</td>
<td>632 ± 154</td>
</tr>
<tr>
<td>Min - Max</td>
<td>22 - 72</td>
<td>56 - 116</td>
<td>200 - 386</td>
<td>1.9 - 4.5</td>
<td>315 - 828</td>
</tr>
<tr>
<td><strong>Whole body - 5 females</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean ± SD</td>
<td>57.6 ± 18.7</td>
<td>69.3 ± 29.7</td>
<td>223 ± 86</td>
<td>2.7 ± 1.8</td>
<td>474 ± 335</td>
</tr>
<tr>
<td>Min - Max</td>
<td>37 - 79</td>
<td>47 - 103</td>
<td>155 - 361</td>
<td>1.2 - 5.5</td>
<td>193 - 1019</td>
</tr>
</tbody>
</table>

The first columns for each exam on the graph represent the CT contribution to $E$, the second columns describe $E$ from the PET component, applying ICRP 80 conversion coefficients, the third columns describe $E$ from the PET component, applying Andersson’s coefficients [10], and the fourth columns show the total $E$, taking into account the radiopharmaceutical contribution, calculated with ICRP 80, for consistency with the national survey.

![Graph showing effective doses from standard and whole body PET-CT examinations](image)

**Figure 1.** Effective doses from standard and whole body PET-CT examinations. The first column for each exam represent the CT contribution to effective dose in millisievert, the second column describes effective dose from the PET component, applying ICRP 80 conversion coefficients, the third column describes effective dose from the PET component, applying Andersson’s coefficients [10], and the fourth column shows effective dose from the whole examination, taking into account the radiopharmaceutical contribution, calculated with ICRP 80. Patient data are included for the sample of 50-90 kg body weight.
The administered activity doesn’t depend on the type of examination (standard or whole body), but only on patient’s weight (usually 3 to 3.5 MBq kg\(^{-1}\) are injected). Therefore the same data with good statistics of the RPh contribution to \(E\) from the standard exam were used for calculation of the total \(E\) for both types of examinations. This contribution was 4.4 mSv with ICRP 80 conversion coefficients. \(E\) from the RPh, estimated with Andersson’s coefficients, was 3.7 mSv, 16% lower than the value with ICRP 80 coefficients. It is expected that the latter estimation is more realistic, taking into account the use of voxel phantoms, based on real humans, new decay data, and new tissue weighting factors, for the derivation of the conversion coefficients. The mean activity over both males and females (50-90 kg) was 230 ± 34 MBq. If calculation of RPh contribution to \(E\) is performed for the whole patient sample of 120 patients, all weights, for the standard exam (mean weight 74.7 ± 19.8 kg, and mean activity 248 ± 63 MBq), the RPh contribution to \(E\) is estimated 4.7 mSv. This contribution from the national survey was 4.9 and 5.9 mSv for patients with mean weights 72.8 ± 13.9 and 74.0 ± 17.3 kg respectively, on both systems, participating in the survey. The values from the present study are lower, especially in comparison with the second system, although the mean weight is slightly higher.

Mean CT\(D\)\(I_{vol}\) for the standard examination over both sexes (50-90 kg) was 2.4 ± 0.9 mGy, the mean DLP was 261 ± 102 mGy cm. The CT contribution to \(E\) was 3.6 mSv. These statistics for the whole sample, all weights, were mean CT\(D\)\(I_{vol}\) 2.8 ± 1.4 mGy, mean DLP 303 ± 154 mGy cm, and CT contribution to \(E\) of 4 mSv. These data for both systems from the national survey were for CT\(D\)\(I_{vol}\) and DLP as follows: 5.9 ± 1.0 mGy and 5.4 ± 2.0 mGy, and 591 ± 130 mGy cm and 575 ± 248 mGy cm respectively. The corresponding CT contribution to effective dose was 7.8 and 7.7 mSv. The CT doses from the present study, standard examination, are about 49% lower for the whole sample of patients in comparison to the other two PET-CT systems. Total \(E\) from the standard examination was 8.0 mSv for the 50-90 kg patient sample and 8.7 mSv for all weights patients.

CT contribution to \(E\) for the whole body examination was 4.7 mSv (9.4 and 5.9 mSv were reported from the national survey). The RPh contribution was estimated using the same data as for the standard exam (4.4 and 3.7 mSv using the old and the new conversion coefficients respectively, 50-90 kg weight), and the total \(E\) was 9.4 mSv, taking into account the RPh contribution from patients with all weights. Total \(E\) from the whole body examinations from the national survey was 14.5 and 11.8 mSv for both systems.

Total \(E\) values, calculated from the present study (whole sample of patients, all weights) and from the previous national survey, are presented on Figure 2 and Figure 3 for standard and whole body examinations respectively. The SPECT-CT system from the present study is denoted as III. Total effective doses on the new system are between 20% and 36% lower for the different types of examinations, in comparison to the other systems in the country. Several factors influence the lower doses on system III. It is a quite new system on the market that uses the latest technologies.
Figure 2. Comparison of total effective doses in millisievert, received by patients from PET-CT standard examinations, for patient samples, including all weights. Effective dose from the new system III is 32% and 36% lower compared to systems I and II respectively.

Figure 3. Comparison of total effective doses in millisievert, received by patients from PET-CT whole body examinations, for patient samples, including all weights. Effective dose from the new system III is 35% and 20% lower compared to systems I and II respectively.

The PET detectors (LightBurst technology) are more sensitive and new reconstruction algorithms are provided, both allowing the use of lower injected activities. The new iterative reconstruction algorithm for PET images Q.Clear is still not used on a routine basis. Even lower activities could be expected after its use becomes standard practice. The CT scanner is also using more sensitive detectors. The Adaptive Statistical Iterative Reconstruction (ASiR) algorithm for the CT is present, but it is not used for image reconstruction in the scanning protocols yet. Its introduction is expected soon, with further
decrease of CT doses.

National survey of patient doses from whole body PET-CT imaging with $^{18}$F-FDG was performed in France in 2011 \[17\]. It included about 1000 examinations of patients weighing 50-100 kg on 56 PET-CT units. The average reported activity was 301 MBq, with diagnostic reference level (DRL) in the country 350 MBq. For new systems, equipped with the “time-of-flight” (TOF) technology, the mean activity was 250 MBq. The average activity was reported to correspond to 5.7 mSv effective dose, applying the same conversion coefficients as in the present study, published by ICRP 80/106/128. The CT contribution to $E$ in the study was estimated with the same software CT Expo. The average CTDI$_{vol}$ and DLP were reported to be 6.6 mGy and 628 mGy cm respectively, with contribution to $E$ of 8.6 mSv. Total mean effective dose was assessed to be 14.3 mSv, higher than this value for all Bulgarian systems. Another recent study explored the variability of administered activity of $^{18}$F-FDG in Europe, Australia and the USA, based on 24 716 PET examinations in 15 centres \[18\]. The mean activity was 340.3 MBq, median for TOF scanners was 243.8 MBq, and for non-TOF scanners the median was 552.1 MBq. The effective dose per patient from the RPh, based on ICRP 80/106/128, varied between 4.6 and > 11 mSv. Survey in the USA, published in 2015, based on 95 PET facilities, reported average activity 508 ± 117 MBq, range 108-875 MBq \[19\]. A European study under the project Dose DataMed II reported from 289 up to 400 MBq mean administered activities in European countries, the mean value for whole Europe was 345 MBq, average $E$ from the $^{18}$F-FDG, tumor imaging, was 6.7 mSv \[20\]. DRLs from this report for 7 countries varied between 350 and 400 MBq. Jallow et al. performed a study on CTDI$_{vol}$ from 282 PET-CT systems in the USA between 2010 and 2014 \[21\]. The mean values per year were between 6.8 and 7.5 mGy, much higher than in this study. In summary patient doses, estimated in the present study from both RPh and CT are low, compared to several big studies. The activities applied in the new hospital are comparable with the reported activities for systems with the new TOF technology. This technology is not available in this scanner, but other dose saving options are present instead, achieving similar dose levels from the RPh. Even so when the full potential of the PET-CT system will be used, further decrease of doses can be expected.

Conclusions

Patient doses from whole body tumor imaging with $^{18}$F-FDG on the new PET-CT system, installed in Bulgaria, were determined. These data supplemented the information from the first national survey of patient exposures from hybrid imaging in nuclear medicine. Effective doses from both radiopharmaceutical and CT contribution were found to be quite low, with a total effective dose from the standard examination of 8 mSv, and from the whole body examination – 9.1 mSv, for patients with mean weight. Even further reduction of patient exposures is expected when all dose saving options of the PET-CT scanner will be implemented in practice. Smaller contribution to the dose of the PET part of the examination is estimated when the new and more realistic conversion coefficients are used. Effective doses, received by patients in Bulgaria from PET-CT examinations, are lower or comparable to doses from other well developed countries.
References:


SURVEY OF PRACTICE AND DOSE OPTIMISATION STRATEGIES IN PAEDIATRIC PET/CT PROCEDURES

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Abstract

The use of hybrid imaging technologies such as PET/CT systems is rapidly expanding. The radiation doses delivered to patients undergoing PET/CT are relatively low, but repeated procedures may lead to significant cumulative doses. This is of a particular concern for paediatric patients, because of their higher tissue radiosensitivity and longer life expectancy.

The purpose of this survey was to estimate paediatric patient doses from PET-CT procedures and to explore potential for optimisation. Data were retrospectively collected for 123 paediatric patients examined with the system GE Discovery 600 during the period 2014-2016. The following parameters were recorded for all patients: indication and type of examination; patient’s age, weight, height and gender; tube voltage (kV); tube current (mA); pitch; rotation time; slice width and number of frames; CTDIvol; administered activity of the radiopharmaceutical 18F-2-fluoro-2-deoxy-D-glucose (FDG). Two types of examinations were performed: whole-body or head. Large variations in CTDIvol, up to 5, were found within one of the age groups. For head examinations the average CTDIvol varied between 1.8 and 2.2 mGy for different age groups. The average administered activity for the same type of examination varied between 123 and 187 MBq (the lowest value was observed in the age group 5-9 y). Pure correlation was found between administered activity and patient weight.

The average CTDIvol for the whole body PET/CT varied between 1.2 and 3.8 mGy. The average administered activity varied between 90 and 279 MBq. For this examination strong correlation was found between administered activity and patient weight for all age groups except 1-4 y. Automatic exposure control was used for all the patients, types of examinations and body regions. Good practice for patient dose registration and records has been observed.

A potential for optimisation of procedures was found. Recommendation was given for proper selection and registration of the exposure parameters for the CT part of examination according to patient age and weight. Low dose paediatric head CT protocols should be developed. A protocol for appropriate manipulation and administration of radiopharmaceuticals according to patient’s weight should be implemented and reduction of total exposure time in the department.
Introduction

The use of hybrid imaging technologies such as positron emission tomography co-registered with computed tomography (PET/CT) systems is rapidly expanding. The main advantage of PET/CT systems is the superimposition of a metabolic functional PET image with anatomical CT image of high contrast resolution. The use of PET/CT in adult oncology, neurology and cardiology is well established. However, experience with PET-CT in the field of paediatric imaging is limited. It is not possible to apply the same selection criteria for adult and paediatric imaging. In rare conditions, the routine use of PET/CT cannot be recommended but PET/CT may be able to assist in individual management by resolving clinical questions that are difficult to answer using anatomical imaging alone.

There are two main components defining the exposure from PET/CT examinations. The first component is the exposure from the administered radiopharmaceutical, usually 18F-2-fluoro-2-deoxy-D-glucose (FDG), which causes an internal irradiation of the patient. The other component is the external exposure from the x-ray tube of the CT component of the system. These two different components of the PET/CT medical examinations, both of them involving ionizing radiation, result in an increased exposure for the patient. For these reasons the hybrid imaging technologies are typically performed with low dose CT scan protocols (low kV and/or mAs), in which the CT is mostly used as an anatomical reference for the PET acquisition, except when a diagnostic CT scan is also necessary. The effective doses from the PET component are significantly lower compared to diagnostic CT examination and they depend on the activity of the administered radiopharmaceutical. The administered activity cannot be reduced significantly, because its amount is defined by patient’s weight. Patients’ exposure from PET/CT examinations can be significantly reduced by optimised routine CT protocols and adjusted exposure parameters according to patient’s age and weight.

For children should be first individually evaluated if a low-dose CT should be used for attenuation correction and anatomic localization only, or a diagnostic routine-dose CT should be used instead.

The CT tube current values may be reduced to 25–35 mAs and lower (pitch, 1.5) for most CT scans for children, used for attenuation correction and localization only [1]. According to the literature, different researches indicate that if the CT scan is performed for anatomic localization of the PET image only, the acquisition technique parameters could be reduced substantially from diagnostic levels, often by 50-80% [2,3,4]. Furthermore, if the CT study is only necessary for attenuation correction of the PET image, the technique parameters could be reduced even further, leading to reduction of the parameters with a 10-100 times the diagnostic CT levels [5,6]. For the purpose of PET attenuation correction, the CT image is used to generate a low resolution attenuation map. Thus CT images used for attenuation correction could be with higher noise, compared to diagnostic quality images, as they would be smoothed to match the PET resolution, prior to the generation of PET attenuation correction factors.

Different studies show that the radiation exposure of patients undergoing PET/CT are relatively low, but repeated procedures may lead to significant cumulative doses [2,5,6]. This is of a particular concern for paediatric patients, because of their higher tissue radiosensitivity and longer life expectancy. The purpose of this survey was to estimate paediatric patient doses from PET-CT procedures and to study potential for optimisation.
Materials and Methods

Data were retrospectively collected for 123 paediatric patients examined with the system GE Discovery 600 during the period 2014-2016. The following parameters were recorded for all patients: indication and type of examination; patient’s age, weight, height and gender; tube voltage (kV); tube current (mA); pitch; rotation time; slice width and number of bed positions; CTDIvol; administered activity of the radiopharmaceutical FDG.

Results

The patient distribution by age and type of examination is shown on fig. 1. 44 paediatric patients were between the age of 15 and 19 years and they were selected to be defined as the “young adults” group representatives.

![Figure 1. Patient distribution by age and type of examination.](image)

Indications for paediatric PET/CT imaging

Studies have demonstrated many paediatric tumours to be FDG-avid; up to now, no paediatric tumour has been identified as ‘non-FDG-avid’. With the exception of Hodgkin’s lymphoma no clear guidelines exist. Different studies suggest that FDG-PET/CT could be used to enhance the care of children with cancer. In general, the most common indications for performing an 18F FDG scan on children in the Department of Nuclear Medicine of the corresponding author’s institution could be divided into the following four groups:
1. **FDG PET/CT for initial diagnosis, staging and restaging purposes in oncology:**

The ability of PET/CT to answer clinical questions during a patient’s treatment course may be greatly enhanced by the presence of a scan at the time of diagnosis, before treatment begins. However, it is clearly not appropriate for all children to have a pre-treatment scan. Pre-treatment PET/CT scans should be considered for any child with: Hodgkin’s lymphoma (on or off trial), Non-Hodgkin’s lymphoma with unusual primary or metastatic sites, Extra-medullary leukaemia, Malignancy with unknown primary, Soft tissue sarcoma – for staging, Bony sarcoma with extra-pulmonary metastatic disease, MIBG-negative neuroblastoma, Opsoclonus myoclonus syndrome with no identified primary, Germ cell tumours, Langerhans’ cell histiocytosis (multisystem) and other.

2. **FDG PET/CT treatment related scans in oncology:**

Before local therapy, FDG-PET scans should be considered for children who are candidates for radiotherapy (for conditions known to be FDG-avid), hepatoblastoma requiring liver transplant, Wilms’ tumour considered for bilateral renal surgery (to assist nephron sparing), Stage 3 neuroblastoma after initial chemotherapy (if further chemotherapy is under consideration for further tumour reduction), Mutilating sarcoma surgery. Treatment response scans should be considered in any child with Hodgkin’s lymphoma (as per EuroNET protocol, for children on and off trial), Non-Hodgkin’s lymphoma with poor response on conventional imaging MIBG-negative neuroblastoma, Langerhans’ cell histiocytosis, Soft tissue sarcoma.

3. **FDG PET/CT for follow up in oncology:**

Scans for follow-up are only advisable if prompt further life-saving treatment is planned in the event of relapse/progression. Scans may be considered for any child with confirmed or suspected relapse of above conditions.

4. **FDG PET/CT indications in neurology:**

In the investigation of epilepsy, FDG PET/CT scanning could be considered if the child has focal epilepsy that is potentially amenable to surgical intervention, where MRI is negative or discordant with other investigations. Additional supportive evidence from FDG PET/CT may then justify more invasive procedures such as invasive electroencephalogram (EEG) monitoring to localise seizures with sufficient certainty to warrant surgical resection. In practice where the clinical, EEG and structural data are all concordant, FGD PET/CT is likely to be unnecessary.

Judicious use of PET/CT scans may be considered in the management of patients with neurofibromatosis 1 with symptoms suggestive of malignant transformation of a plexiform or subcuteaneous neurofibroma.

**Patient preparation**

A successful PET scan should always begin with appropriate patient preparation. In the Department of Nuclear Medicine a specific information is required for optimal interpretation of FDG PET/CT images, such as clinical history; results of previous imaging studies; history of surgery, chemotherapy, or radiation therapy. Full information and explanation of the procedure shall be given to the patient and his/her parents [7]. The parents
and patients could be confused by the complexity of the procedure, so they are informed and have the opportunity to ask additional questions. On arrival in the nuclear medicine department, the patient’s height and weight are obtained. The child should fast for at least 4–6 hours before the study. Patients should drink water to maintain good hydration if there is no indication for anaesthesia or sedation [8,9]. It is often preferable to give a short duration anesthetic than to administer sedation, as sedation can be unpredictable in children. Intravenously performed hydration during the uptake period may be achieved with 0.9% saline solution. For infants, radiotracer injection should be timed as close as possible to breast or bottle feeding; a feed may be given from 30 minutes after injection [8,9]. The fasting blood glucose level needs to be determined prior to 18F FDG injection, with the preferred level being lower than 7 mmol/L [8]. If the blood glucose level is higher than 7 mmol/L, the supervising physician should be notified so that a decision can be made whether to proceed with the radiotracer injection. Local anaesthetic cream can be used to reduce the discomfort caused by the intravenous catheter. Children with known or suspected tumours are usually imaged approximately 1–2 hours after the intravenous administration of 18F FDG [8]. The optimal 18F FDG distribution phase is controversial. The duration of the 18F FDG uptake period should be kept constant whenever possible. The injected activity should be adjusted to the patient’s weight and to the type of acquisition. After injection, children should avoid exercising, talking, or chewing. They should be kept warm during the uptake phase with an adequately heated room and, if it is needed, the use of warm blankets or clothing. This approach may help reduce radiotracer uptake in thermogenic brown fat. At the corresponding author’s institution, children spend the uptake period in a warm, quiet room where they lay relaxed. The uptake period for children is about 45 minutes. After the uptake period, the patient is positioned on the table for the examination where anaesthesia is given, in case necessary. After the anaesthesia, the anaesthesiologist monitors the patient breathing through a window in the PET/CT control room.

The need for a sedative or anaesthetic must be assessed on a case-by-case basis for children who cannot remain motionless in the scanner for at least 15–20 minutes. Patient motion will compromise the PET study, resulting in inadequate image quality. Generally, sedation or anaesthesia protocols are variable and are performed in accordance with institutional guidelines.

**Nuclear medicine practice and patient’s dose results**

Established practice within the corresponding author’s institution is as follows: for head examinations a field of view (FOV) including the skull and the shoulders is used while for whole body examinations a FOV extended from the skull to the midthighs is usually sufficient. The median values of the numbers of used bed positions for the different age groups and type of examinations are as follows: 2 for all head PET/CT examinations, 7 for (1-4 y) and (5-9 y), 8 for (10-15 y) and 9 for “young adults” whole body PET/CT.

Within the study, automatic exposure control (AEC) was used for all the patients, types of examinations and body regions. Good practices for patient dose registration and its records were observed.

The review and the analysis of the routine protocols used, as well as the prescribed CT (low-dose or diagnostic CT), showed that a low dose CT was almost never used. The routine protocols were adjusted with a tube voltage between 100 and 120 kV and upper limit of the tube current, and tube current modulation within the upper limit between 110 and 250 mA, in accordance with the selected protocol and lower limit of the tube current modulation of 30 mA. All patients were scanned with a pitch factor of 1.375, rotation time of 0.8 s and
body bow-tie filter. The paediatric protocols were not optimised and some of them were adjusted with the same typical adults’ exposure parameters. The routine paediatric CT protocols were not designed for attenuation correction and anatomic correlation of the PET findings. Patients were often referred for low-dose CT procedures but were imaged with the diagnostic CT protocol.

In case anatomic correlation of the PET image is not necessary, lower tube voltages and tube currents could be used without degradation of the attenuation-corrected PET images.

Large variations in CTDI\text{vol} and DLP, up to 5 times, were discovered within the results for whole body PET/CT for one of the age groups (10-15 y) (fig. 2 and 3). The median value for CTDI\text{vol} for the whole body PET/CT varied between 1.2 mGy and 3.8 mGy for the different paediatric age groups. The same variations were found also for adult examinations, more than factor of 5, with median value for CTDI\text{vol} of 3.4 mGy (1.8-10.2). For head examinations the median CTDI\text{vol} varied between 1.8 and 2 mGy for different age groups (fig. 2). The median of the DLP values for head PET/CT was in the range 44.2 - 48.6 mGy.cm and 97-225 mGy.cm for whole body examinations (fig. 3). The median values for DLP for adult head and whole body PET/CT were 44 mGy.cm and 365 mGy.cm respectively.

Fig. 2. CTDI\text{vol} values for the different age groups for head and whole body PET/CT examinations.
Fig. 3. DLP values for the different age groups for head and whole body PET/CT examinations.

Pure linear correlation was found between administered activity and patient weight for head PET/CT (R² in the range 0.11-0.37). The median of the administered activity for the same type of examination varied between 129 MBq and 180 MBq (with lowest values observed in the age group 5-9 y) while median value of the administered activity for adult patients was 196 MBq.

Large variations were also observed for the average applied activity per patient’s weight within the youngest age groups. The results are presented on fig. 4. Decrease of the administered activity per kg weight is observed with the increase of patient’s age. The median value of the administered 18F-FDG activity per kilogram patient’s weight was 7.8 MBq/kg for age group (1-4 y), 4.8 MBq/kg (5-9 y), 3.5 MBq/kg (10-15 y) and 1.1 MBq/kg for adult patients. The average 18F-FDG per kg activity for adults’ head PET/CT was over 7 times lower than the respective value for the youngest patients. The study showed that a proper protocol for appropriate manipulation and administration of radiopharmaceuticals according to patient’s weight, is not defined. A dose of 3-6 MBq/kg is recommended for paediatric oncology patients, according to the mode scanning acquisition - 3D or 2D respectively [9]. The results from the subject survey showed that only for age group (1-4 y) activity higher than 6 MBq/kg was used for head examinations, but all children under the age of 15 years were injected with activities higher than 3 MBq/kg.
Fig. 4. Administered $^{18}$F-FDG activity per kilogram patient’s weight for the different age groups for head and whole body PET/CT examinations.

The median value for the administered activity for whole body PET/CT varied between 87 and 180 MBq for the different non-adult age groups. For this examination strong correlation was found between administered activity and patient weight for all age groups except 1-4 y. The median value for the administered activity for whole body adult PET/CT was 275 MBq. Smaller variations, up to factor of 3, are observed for the average applied activity per patient’s weight, within the different age groups, when compared to the variations for head examinations (fig. 4). The same trend of decrease in the quantity of administered activity per kg with the increase of patient’s age is observed.

The evaluated median values of the administered $^{18}$F-FDG activity per kilogram of patient’s weight are as follows: 5.1 MBq/kg for age group (1-4 y), 4.3 MBq/kg (5-9 y), 4.1 MBq/kg (10-15 y) and 1.6 MBq/kg for adult patients.

The average $^{18}$F-FDG activity for adults’ whole body PET/CT is over 3 times lower than the respective value for the youngest patients. The results from the performed survey
for whole body PET/CT showed that all paediatric age groups exceed the recommended 3 MBq/kg activity. Activity lower than 3 MBq/kg is used only for adult patients. All age groups, paediatric’s and adult’s, do not exceed the 6 MBq/kg level.

**Conclusions**

Substantial potential for optimisation of the PET/CT procedures is identified, based on the performed study results. Recommendations for improvement include proper selection and registration of the exposure parameters for the CT part of examination, according to patient age and weight. Low dose paediatric head CT protocols should be developed. Imaging procedure for children should be defined on individual basis, in order to determine if a low-dose CT is to be used for attenuation correction and anatomic localization only, or diagnostic routine-dose CT should be used instead. The use of routine optimised protocols, adapted to patient’s age and weight, allows the adjustment of acquisition settings to minimize patient’s exposure while maintaining diagnostic image quality. A protocol for appropriate manipulation and administration of radiopharmaceuticals, according to patient’s weight, should be established, as well as optimisation procedures for total exposure time in the studied department. The survey and optimisation process is still in progress. The purpose of ongoing studies is to define optimal exposure CT parameters, minimal PET acquisition durations and administered activities for each patient category.
References:

MTF AND CONTRAST INVERSION

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Assessment of the limiting spatial resolution with a test object is a routine operation during Quality Control (QC) in X-ray diagnostic radiology. During this operation one can observe inversion of contrast of the images of test patterns (visual “negative” structures). These “negative” structures are visible for objects with spatial frequency above the limiting spatial resolution.

The presentation explains the geometry and mathematics of contrast inversion in these cases. The mathematical extraction of the Modulation Transfer Function (MTF) from the image geometry is shown. The result, MTF as a decaying sine function, makes clear the contrast inversion. While for the QC purposes only the modulus of MTF is taken into consideration, the remaining parts of the decaying sine function lead to contrast inversion of the still visible small patterns. In some cases one can observe even two consecutive contrast inversions.

The contrast inversion effect can confuse the assessment of the limiting spatial resolution through the observation of the test object patterns (with increasing spatial frequency). However, and more importantly, this effect can confuse the visualisation of small objects in the medical image during digital X-ray radiography. This effect is also one of the reasons for increased noise in digital radiography images.

Understanding the contrast inversion mechanism can be useful for the development and assessment of software for automatic QC.

- Key words: modulation transfer function, image quality assessment, quality control
EDUCATION AND TRAINING RELATED TO ANTHROPOMORPHIC PHANTOMS FOR MEDICAL PHYSICS EXPERTS

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In 2013, a new ambitious unique project related to qualification of Medical Physics Experts in Diagnostic and Interventional Radiology started. The EUTEMPE-RX project aimed at development of a course composed of 12 educational modules, providing a training scheme that allows the medical physicists in Diagnostic and Interventional Radiology to reach a high level of knowledge, skills and competences.

The EUTEMPE-RX project has been completed but its sustainability plan assured the continuation of the education of Medical Physics Experts. One of the 12 modules, the “Physical and virtual anthropomorphic phantoms for image quality and patient dose optimization”, is developed and taught at the Technical University of Varna. It provides education and training in the field of design, implementation and use of anthropomorphic phantoms in virtual clinical trials including existing and new Diagnostic and Interventional Radiology technologies.

The current paper presents the content of the module – the e-learning and face-to-face parts, and its impact on the participants. The online e-learning part includes 10 chapters with state of the art reviews in the field of physical and computational anthropomorphic phantoms, introduction and tutorials to software applications for design of phantoms and their use with x-ray imaging techniques with examples. The material for the online part was initially developed and stored on the SEKOIA platform and then migrated and made available on a MOODLE platform. The next face-to-face part of the “Anthropomorphic Phantoms” module will start on 22 May 2017 at the Technical University of Varna, and will last for 5 days. This part is organized in a blended format that includes lectures, computer-based exercises, a visit to the hospital for experimental work, discussion sessions and project work. The focus is given on practical work and development of a work project. Module assessment includes implementation of a work project on a case study from Diagnostic and Interventional Radiology, combined with a short written exam.

All lectures are led by worldwide recognized researchers in the field of anthropomorphic phantoms and their use in the research and clinical practice.

• Key words: medical physics education, anthropomorphic phantoms, computer simulations, virtual clinical studies
Computed Tomography (CT) is an essential and widely utilized tool for diagnosis in today’s medicine, and there are a variety of tools we can employ in order to optimize and track dose among multiple scanners and multiple facilities. CT is also a complex tool that requires proper understanding of its capabilities and knowledge of image formation, image processing, and radiation dose, and as a result, training of technologists is crucial. Ensuring consistency across multiple facilities can be challenging because of differences in equipment, staff culture and radiologist preferences. This paper intends to present our efforts to track CTDI$_{vol}$ across facilities, to benchmark, and to optimize the CT protocols. With the help of the Radimetrics dose tracking software, we are able to find suboptimal practices and correct them, compare CTDI$_{vol}$ among facilities, track and analyze protocol changes. Another tool that assists in preventing too high a patient dose is Dose Check, which informs the technologist if the planned scan would exceed established reference levels, allowing the technologist to judge whether this is appropriate. Employing Dose Check has been helpful in keeping the patient exposure below the established reference levels. Since the CT technologists are on the front lines of controlling patient dose, training requirements have been updated to better reflect the need of expertise in the field. All of these activities are under the guidance of the hospital CT Task Group, which includes radiologists, technologists, administrators and the physicist. Optimizing dose to patients from CT is a multidisciplinary problem and our team approach has lead to positive results.

- **Key words**: computed tomography; CT dose tracking; CT dose optimization
STRATEGIES FOR MINIMIZING PATIENT RADIATION DOSE IN INTERVENTIONAL FLUOROSCOPY

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Interventional procedures are performed in different clinical areas, such as surgery, cardiology and radiology. They are performed under the guidance of interventional fluoroscopic devices. These devices have numerous protocol setting, image processing and acquisition options. Complex procedures can often last a very long time and thus increase the probability of inducing damage to the skin. Many factors can contribute to the radiation exposure to patients and the possible effects from it, such as patient weight, age, gender, prior interventional exams, and certain medical conditions. It is important to plan each procedure carefully and to consider modifying it in order to minimize skin damage. Patient education and follow-up is very important when certain thresholds are reached and adverse effects are possible. This paper presents several strategies that help reduce patient exposure during interventional procedures.

\textbf{Key words:} interventional fluoroscopy
COMPARISON OF 3D CONFORMAL RADIOTHERAPY AND HELICAL TOMOTHERAPY FOR IRRADIATION OF THE BREAST AND THE REGIONAL LYMPHATICS

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**Purpose:** To compare new treatment planning protocol for left and right site breast irradiation, when the planning target volume has to include the involved breast (PTV) and supraclavicular lymph nodes (PTV_SCLN) using helical tomotherapy and routine “one isocenter” 3D conformal radiotherapy technique.

**Methods and Materials:** Ten left and ten right breast patients were planned for prescribes dose 50 Gy. 3D CRT plan was created with an isocenter situated at the lower edge of the supraclavicular part of the target volume, and asymmetrical MLC collimated beams. Tomo Helical plan was developed with field width –5.048 cm, pitch 0.22 cm and modulation Factor 3. The fall-off of the dose was controlled by help contours at a distance of 1.5 cm form PTV and PTV_SCLN. Directional blocking was applied to heart and contralateral breast and lung.

**Results:** The outcomes for Tomo helical vs. 3D CRT are listed below: For PTV: Dmin (2ccm) 39.7 ± 1 Gy vs. 25.9 ± 6 Gy, Dmax (2ccm) 52.7 ± 0.4 Gy vs. 54.51 ± 0.6 Gy, V95% 48 ± 1 Gy vs. 44 ± 1.5 Gy; For PTV_SCLN: Dmin (2ccm) 45.4 ± 0.6 Gy vs. 37.8 ± 1.6 Gy, Dmax (2ccm) 51.8 ± 0.2 Gy vs. 55.2 ± 0.6 Gy, V95% 48.9 ± 1 Gy vs. 45.2 ± 1.5 Gy. With both techniques ipsilateral lung received the same middle dose - 13 Gy (+0.3 Gy; -0.7 Gy), the volume received 30 Gy is 8.5% higher in the CRT plans but the dose received in 65% of the lung volume is 3 Gy more for Tommo helical. The middle dose for contralateral lung was 3.5 Gy lower for 3D CRT (1.2 Gy vs. 4.8 Gy). Heart’s average dose for left breast cases was 5 Gy higher for helical plans, but in 3D CRT plans Dmax was 10 Gy more and V30 Gy was 3.6% vs 0.6%. The average dose in contralateral breast was 2.5 Gy more in tomo helical plans. The liver in right breast cases with 3D CRT plans got 5 Gy less average dose but 7 Gy more for Dmax.

**Conclusion:** The conformity and homogeneity of PTVs were better for helical tomotherapy plans than the 3D CRT for both left and right breast tumor with regional lymph node involvement. The organs at risk: ipsilateral lung, contralateral lung, contralateral breast, heart and liver received higher average dose in tomo helical plans, but lower maximum dose.

**Key words:** Treatment planning, Breast cancer, 3D conformal radiotherapy (3D CRT), Helical tomotherapy.