REVIEW

of the PhD thesis "Innovative phantoms for image quality research in modern mammographic techniques",

for PHD in 4. Natural Sciences, Mathematics and Informatics, professional field 4.1 Physical sciences, specialty "Medical Physics"

Author: Assoc. Prof. Desislava Zvezdomirova Kostova-Lefterova, PhD

National Cardiological Hospital,

MU-Pleven

The review was prepared on the basis of the following documents provided to me: PhD thesis, abstract, list of publications related to the dissertation, copies of publications, author's curriculum vitae.

The relevance of Yanka Ivanova Baneva's PhD is undeniable - breast cancer (BC) is the leading cause of death from malignancy in women worldwide. The diagnosis of BC is a challenge in modern imaging. This is due to the complex anatomical structure of the breast, the small difference between the densities of glandular and cancerous tissue, and the small size of malignant neoplasms at an early stage, on the order of 0.1-0.15 mm. High-resolution, high-contrast images are needed to diagnose the disease as early as possible. The success of subsequent surgical and conservative treatment of the disease depends on the extent to which the listed criteria for a good diagnostic image are met. Some of the imaging methods are used for screening purposes, others for diagnostic purposes, and still others as a complementary method to refine the diagnosis. Many efforts are continuously being made to improve the efficacy of various imaging methods for the diagnosis of BC. The development of phantoms that can be used to assess image quality is fundamental to improving the diagnostic capabilities of breast imaging methods.

In connection with her thesis work, Yanka Baneva is part of a team that has successfully developed, validated and used innovative computer phantoms to investigate image quality in modern breast imaging modalities such as tomosynthesis and contrast-enhanced mammography. Methods that have the potential to be used for early screening and diagnosis of BC.

The PhD thesis is written in 80 pages of main body and 105 pages in total, which includes an 11-page references, and 3 pages of contributions, lists of publications and scientific communications related to the dissertation, as well as 5 pages of abbreviations and notations used, list of figures and tables.

The largest section is the INTRODUCTION - 27 pages, followed by the sections DEVELOPING AND USING COMPUTER MODELS OF THE MAMMARY GLAND FOR THOMOSYNTHESIS - 12 pages, COMPUTER MODELS OF THE MAMMARY GLAND WITH CONTRAST SUBSTANCES - 11 pages, "IMPACT OF MAMOGRAPHIC SPECTERS AND CHARACTERISTICS OF COMPUTER MODELS OF THE MALIGNANT GLAND ON THE CHARACTERISTICS OF MAMOGRAPHIC IMAGES" - 10 pages, "METHODS USED IN THE PhD THESIS" - 8 pages, "MODELS OF THE MAMMARY Gland FOR X-Ray Studies" - 7 pages, "Conclusion" - 3 pages and "OBJECTIVE" - 2 pages. The work is richly illustrated - it contains 49 figures, some with several separate parts. The number of tables is 19. The structure of the thesis is logical, but its poor formatting in places makes it difficult to read, use and follow the data.

In the section "INTRODUCTION" the author briefly presents the incidence of BC, the types of structures that make up the breast and the problems associated with distinguishing healthy from tumour tissue. The main methods of breast imaging are discussed, as well as their advantages and disadvantages. Towards the end of the section, emphasis is placed on X-ray mammography and clinical findings. Screening for BC is reported and emphasized, but what screening is and what requirements must be met by the patient cohort, the equipment used, and the professionals involved in performing it are not described in details. The development of phantoms and their application is strongly linked to the quality of X-ray beam, which is mentioned but not defined.

In the section "MODELS OF THE BREAST FOR X-RAY STUDIES", Yanka Baneva discusses various physical and computer models of the breast described in the scientific literature.

In the section "METHODS USED IN THE PhD THESIS" the author presents several different software applications that were used for the purpose of the dissertation.

In the section "DEVELOPMENT AND USE OF COMPUTER MODELS OF BREAST PHANTOMS FOR THOMOSYNTHESIS" Yanka Baneva describes in detail the validation of the results obtained from the developed and used breast phantom models. This includes a visual and quantitative comparison of the real and simulated images obtained in conventional mammography and breast tomosynthesis for different phantoms. Results obtained using a software breast phantom that reproduces the structure (shape, size and content) and X-ray image characteristics of the corresponding real physical phantom extremely accurately are presented. Quantitative and subjective comparison between real and simulated planar, and tomographic images from the phantoms show very good correlation. Additional software phantoms with spheres made of fatty tissue (Phantom 3) and polyethylene (Phantom 4) show very similar image results, quantitatively and visually, to those of Phantom 2, where the filling material is water. The use of the software platform is envisaged for the development and exploration of a more realistic physical breast phantom in order to refine its imaging techniques.

In the section "THE IMPACT OF MAMOGRAPHIC SPECTERS AND CHARACTERISTICS OF COMPUTER MODELS OF THE BREAST ON THE CHARACTERISTICS OF MAMOGRAPHIC IMAGES" the PhD student describes the construction of breast phantoms of different thickness and content and their simulated mammographic images using special software platforms. Yanka Baneva evaluates the effect of the spectrum of incident X-ray radiation, its influence on the phantom, and investigates the corresponding parameters calculated from the obtained simulated images. Yanka Baneva's conclusion is that the GGA combination of materials can be used to represent a denser breast, while the GAG phantom reproduces a breast with more fatty content represented. The breast carcinoma gene mutation occurs more frequently in women with hyperdense breasts, suggesting that the features studied can be used as basic parameters in the design of software applications for breast density assessment.

In the section "COMPUTER MODELS OF MALARIES WITH CONTRASTIC MATTERS", differently composed computer phantoms for CESM are designed to objectively and subjectively investigate the visualization of the incorporated cylinders with iodine-contrast material in the resulting images, to see the angiogenesis from the simulated images and to select the most suitable phantom for physical realization. In all three computational models, contrast enhancement was observed in the resulting recombined images. Even in the complex computer model (Phantom 3), the heterogeneous background is very well suppressed, while the intensity of the contrast matter cylinders located in the phantom volume is sufficiently enhanced. The heterogeneous phantom can be used in selecting

the appropriate concentration of iodine contrast matter. Further work includes production of the physical phantoms of the chest and their overall evaluation.

The contributions of the thesis are of a scientific and methodological nature. The main contributions are related to the detailed validation and use of the LUCMFRGen software for applications in mammography and three-dimensional imaging, the evaluation of the effect of the incident radiation spectrum and its influence on the phantom, and the creation of a physical phantom for CESM purposes:

- A methodology was developed to create different computer models of the breast with content defined by the researcher.

- Four sophisticated and innovative computational models of compressed breast with different heterogeneous content were created.

- X-ray images of two of these four computer phantoms were modelled using two methods, planar mammography and tomosynthesis.

- Both backprojection algorithms, a pure high-pass Ramp filter and a modified version of it, were used in reconstructing the images from the models.

- A quantitative evaluation of the simulated and experimental mammographic images from the created computer breast models is presented.

- comparison between 3D images obtained from simulated and experimental images is made.

- a successful validation of the LUCMFRGen software for applications in mammography and tomosynthesis was performed.

- Four innovative computational phantoms of compressed breast were created, which have different thickness and composition.

- A Matlab script was developed to generate the images to model eight mammographic energy spectra - Mo 25, Mo/Rh 27, Mo 27, Mo/Rh 28, Mo 30, Rh/Rh 29, Rh 30, Rh/Rh 31.

- Simulated X-ray images of individual phantoms were obtained for all input spectra.

- the main characteristics of the performance of the different types of material used in the different energy spectra used for the modelling of the breast phantoms were investigated and compared;

- developed a methodology to investigate the effect of compressed breast thickness as a function of different X-ray energies.

- A methodology for extracting descriptors from X-ray images has been developed.

- A relationship between fractal index and β factor as a function of incident radiation has been established.

- Three computer models of the mammary gland have been modelled for the purpose of CESM, which will be used to implement physical ones.

- A methodology for modelling CESM and obtaining simulated images has been developed.

- the difference between phantoms with homogeneous and heterogeneous texture is demonstrated by introducing the contrast parameter to compare the images.

I have main critical remarks to the thesis presented in this way, despite the undeniable contributions of Yanka Baneva and the team with which the main tasks of the thesis were realized. The large number of inaccuracies in the text does not make a good impression. Some of them are purely technical, others are related to unclear translation from foreign literature, and in some places the meaning of sentences is completely lost. What stands out the most is the lack of correct terminology in the Bulgarian language from a physical point of view, which leads to the impression that the basics of physics are not fully and deeply understood by the PhD student.

I will not translate them in English, because they are untranslatable by their meaning in Bulgarian.

- ядрено магнитен резонанс, което е физичното явление, което стои зад метода за образна диагностика, вместо приетото по стандарт „магнитнорезонансна образна диагностика“
- ексозиция, вместо експонация
- средна доза за експозиция, вместо средна жлезиста доза (най-вероятно)
- често се говори за доза, без явно да е дефинирана или упомената коя точна доза има предвид докторантката
- изображения, вместо образи
- х-лъчи, вместо рентгенови лъчи
- стр. 32: „Фокусът също е много важен за яснотата на образа…“. Едно от основните неща, които определя фокусът е разделителната способност на образа. Не съществува общоприет термин „яснота на образа“.
- на няколко места в текста се споменава за „коефициент на проникване на х-лъчите“, коефициент на затихване“, което е некоректен термин. Терминът е коефициент на отслабване.
- „резолюция“, „акуратно“, „калцификации“, „региони на интерес“, „репрезентираме“, „радиационна чувствителност“, “замъгляване“, „качествен контрол“ и други, са термини, които имат свой утвърден български аналог: разделителна способност, точно, калцификати, област на интерес, възпроизвеждаме, лъчечувствителност, размиване (нерязкост), контрол на качеството…
- Твърдения, които не съдържат в себе си ясен физичен или какъвто и да е смисъл, като:
    - „Шумът зависи от тока на снопа лъчи по времето и експозицията.“
    - „Основно ограничение на мамограмите е прикриването на образувнията от нормалната тъкан. Важната роля на нормалната тъкан на гърдата за ограничаване на откриването на рак доведе до усилия за характеризиране на статистическите свойства на анатомията в рентгеновите мамографии [98].“
    - „Формата на хистограмата зависи от моментите на разпределението около средното ниво на разпределение на сивото [100].
    - Фракталният анализ на изображението корелира с неравността на изследваните области на интерес.“

- „Наблюдаваното замъгляване в изображенията е очаквано и се дължи главно на (1) ограничената възможност на ъгъла на сканиращата арка, използван при томосинтезата и (2) поради ***<u>конусовидния тип на рентгеновия лъч</u>***.“
- „… мамограмите трябва да предоставят истинска информация за наличието или не на ракови клетки…“. Мамографията не е микроскопско изследване, за да се твърди, че дава информация за наличие или не на ракови клетки.
- „Дозата, получена при извършване на мамография, зависи от много фактори – размера и анатомията на гърдата, рентгеновото устройство, което се използва за извършване на мамографията, избраните настройки на експозиция на апарата, избраните материали за анодната комбинация, използваните методи [119], [120].“
- „рентгенов лъч“ вместо рентгенов сноп
- „…адекватно проникване в тъканта…“

The bibliography is not arranged and sources are not cited according to the BSS requirements.

The dissertation is based on a total of 4 publications, the rest are scientific communications (). One of them is in an international journal with IF - Physica Medica: European Journal of Medical Physycs. Janka Baneva is first author in three of the publications. Yanka Baneva has listed a total of 5 scientific communications related to her thesis. The list of references used includes 133 titles, 122 of them in foreign languages, with the majority of publications from the last 10 years. The literature review includes all important publications on the subject by reputable authors and by the international organisations concerned.

In conclusion, I acknowledge the analysis done in the dissertation and the compliance with the formal criteria, the significance of its scientific contributions. I highly appreciate the contributions of Yanka Baneva's PhD thesis, but critically her work in relation to the writing, layout and terminological inaccuracies in the text. Despite the errors, not only of terminological but also of physical nature, the contributions are undeniable, as is the application of phantoms in clinical practice to improve image quality in mammography of women with BC. On this basis, I will vote positive for the educational and scientific degree of "PhD" to Yanka Baneva and recommend the honourable members of the Scientific Jury to vote positive as well.

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Reviewer:

Assoc. Prof. Desislava Kostova-Lefterova, PhD