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### Phantom with heterogeneous structure of metastases on the basis of nanocomplex for computed tomograph

V.E. Orel<sup>1</sup>,<sup>2</sup>, A.V. Romanov<sup>1</sup>, T.S. Golovko<sup>1</sup>, G.V. Lavryk<sup>1</sup>, N.A. Yoltukhovsky<sup>2</sup>

National Cancer Institute of the Ministry of Health of Ukraine<sup>1</sup> National Technical University of Ukraine "Igor Sikorsky Kyiv Polytechnic Institute" <sup>2</sup>

In order to comply with ALARA test (as Low As Reasonably Achievable), the lowest possible dose of radiation should be applied without yielding diagnostic parameters. In order to solve the question "how can we go lower", an objective evaluation of image quality is required. This is especially important for iterative reconstruction methods that involve the application of nonlinear processes. Image quality indicators, such as contrast, may be sufficient to evaluate image quality in these scenarios. These indicators, based on model research, have become popular in assessing the computed tomography (CT) image quality of the [2]. Most of these studies were performed using phantoms with a uniform background because of their simplicity and broad availability. However, phantoms having the realistic background texture and damage are highly desirable for image quality assessment in clinical computed tomography, since the anatomical background can affect the performance of CT systems [7]. Although anthropomorphic phantoms are commercially available, they are usually not specific and difficult to adjust for metastases' structure assessment [1].

CT resolution in the detection of small-sized metastases is limited. Metastases' dimensions are often substantially less than 5 mm in diameter.

Existing staff phantoms, that are the part of computed tomograph, do not always meet the technological requirements for assessing the possibilities the possibilities of liver metastases visualization of [5]. Therefore, there is a need to increase the radiation diagnosis efficiency with nanotechnologies and possibilities of the subsequent assessment of the developed technology on phantoms, which would accurately simulate the medical and physical properties of human liver metastases with a view to their CT visualization. New classes of contrast agents for CT created in recent years based on the modern achievements in the field of nanotechnology have the opportunity for more intensive contrasting of the diagnostic interest area in the medical image. They have advantages over the known ones because of low toxicity, possibilities of cell internalization and high X-rays absorption capacity [4].

Based on the above, the purpose of the work is to develop a tissue-equivalent phantom of the liver with metastases and nanoparticles to investigate the contrast of the visualized metastasis images obtained with CT.

## Material and investigation methods

Pig liver was taken as the tissue-equivalent phantom for metastases' images visualization. It was based on the fact that according to the absorption scale of X-rays radiation pig liver had almost no different from the human one [6]. Animal age -2 years, gender - male, liver weight -1.7 kg.

The weight and percent composition of the materials used in the manufacture of artificial metastases are presented in Table. 1. Iron oxide nanoparticles  $Fe_3O_4$  20-40 nm in diameter obtained with electron-beam evaporation and condensation technology in vacuum of inorganic materials were applied in this work. Nanoparticles were made at the E.O. Paton Institute of Electric Welding of the NASc of Ukraine. The form of the manufactured metastases was close to cylindrical one with the base of 3 mm and the height of 5 mm.

The technology of the artificial metastases with nanoparticles manufacture included the fol-

meight und percentage ratio of materials used to simulate arbitration metastases in the liver phantom.								
Material	Weight, g	Percentage ratio, %						
Gelatin (TM "Mriya", Ukraine)	15	65,1						
Formaldehyde (Platinum, Ukraine)	6	26,0						
Safflower oil (Ltd «OR Golden Oil», Uzbekistan)	2	8,7						
Nanoparticles Fe <sub>3</sub> O <sub>4</sub>	0,05	0,2						

Table 1.
 Weight and percentage ratio of materials used to simulate artificial metastases in the liver phantom.

lowing steps: 15 g of dry K-17 gelatin was dissolved in 100 ml of 90°C water. After cooling to 50 ° C., 2 ml of safflower oil, 6 g of formaldehyde and 50 mg of iron oxide nanoparticles (Fe<sub>3</sub>O<sub>4</sub>) were added to the gelatin solution. After stirring until the complete dissolution of components, the solution was left for 12 hours for gelation in the room with 20°C. After the full congealing of the mixture, the metastases similar to cylinder form with the base ~ 3mm and the height ~ 5mm were made (Fig. 1).



**Fig. 1.** Artificial metastases primary bursts of: 1,4 – artificial metastasis with nanoparticles; 2.3 – artificial metastasis without nanoparticles.

Artificial metastases were added to the liver by surgical way and placed in the liver. For this purpose cylindrical holes with 5 mm in diameter and 7 mm deep were created. Metastases were arranged in one line for 3 units with a step of 10-15 mm (Fig. 2, 3). In the left part of the liver six artificial metastases without nanoparticles were placed; in the right side of the liver – nine artificial metastases based on the nanocomplex.



**Fig. 2.** Location of artificial metastases in the liver phantom:  $\bigcirc$  – schematic image of metastasis without iron oxide nanoparticles;  $\bigcirc$  – schematic image of metastasis with iron oxide nanoparticles. Geometric dimensions are in mm.



**Fig. 3.** Adding of the artificial metastases to the pork liver.

N₂	1	2	3	4	5	6	7	8	9	Avg
Contrast, ref. unit	0,148	0,063	0,085	0,064	0,046	0,040	0,016	0,052	0,027	0,060 ± 0,014

 Table 2.

 Contrast of the artificial metastases with nanoparticles image at liver phantom CT.

After placement, they were completely covered with hepatic tissue. The prepared phantom was filled with physical solution until its total immersion to simulate the X-rays scattering and absorption at investigations.

Phantom visualization with X-ray irradiation was performed on the CT unit Toshiba Aquilion 16. Voltage and current on the tube were 120 kV and 200 mA, respectively. Contrast media was chosen as the parameter for the evaluation of phantom images quality [8].

# Results and their discussion

The phantom image obtained with CT is demonstrated on Fig. 4.



**Fig. 4.** *CT* zones of the liver phantom with artificial metastases: a – without nanoparticles; b – with nanoparticles.

The visual analysis of the images evidenced that artificial metastases in the left part of the liver without nanoparticles were almost not visualized, while all nine artificial nanoparticle metastases in the right part were clearly visualized on the tomogram. Table 2 demonstrates the calculation of the contrast for images of metastasis with nanoparticles in phantom. The greatest value of the contrast of the artificial metastases visualized by CT was 0.148, and the least -0.016.

### Conclusion

Research on the visualization of liver metastases phantom with nanoparticles by CT demonstrated that artificial metastases of  $\sim 5$  mm in diameter with nanoparticles were clearly visualized in contrast to artificial metastases without nanoparticles which were practically not visualized.

This indicates the appropriateness of combining the methods of malignant tumors radiation diagnosis and nanotherapy with application of nanoparticles as active agents [3], that in prospect may be used in preclinical studies *in vivo* and subsequently brought to clinical practice.

#### Література

1. Construction of realistic liver phantoms from patient images using 3D printer and its application in CT image quality assessment / S. Leng, L. Yu, T. Vrieze [et al.] // Proc. SPIE Int. Soc. Opt. Eng. 2015. – 2015. – Vol. 94124E. [електронний pecypc] DOI: 10.1117/12.2082121.

2. Correlation between model observer and human observer performance in CT imaging when lesion location is uncertain / S. Leng, L. Yu, Y. Zhang [et al.] // Medical Physics. - 2013. - Vol. 40(8). - P. 081908. DOI: 10.1118/1.4812430.

3. Magnetic properties and antitumor effect of nanocomplexes of iron oxide and doxorubicin / V. Orel, A. Shevchenko, A. Romanov [et al.] // Nanomed. Nanotech. Biol. Med. – 2015. – Vol. 11, N 1. – P. 47-55.

4. Nanotechnology and diagnostic imaging: new advances in contrast agent technology / J. E. Rosen, S. Yoffe, A. Meerasa [et al.] // J. Nanomed. Nanotechnol. – 2011. – Vol. 2, N 115. – P. 1–12. doi:10.4172/2157-7439.1000115.

5. Porcine ex vivo liver phantom for dynamic contrast-enhanced computed tomography: development and initial results / S. M. Thompson, J. C. Ramirez-Giraldo, B. Knudsen [ et al.] // Invest. Radiol. – 2011. – Vol. 46, N 9. – P. 586-593.

6. Primary fracture immobilization as a method to prevent post-traumatic pulmonary changes- an experimental model / I. Jansson, R. Eriksson, S. O. Liljedahl [et al.] // Acta Chir. Scand. – 1982. – Vol. 148, N 4. – P. 329-338.

7. Solomon J. Quantum noise properties of CT images with anatomical textured backgrounds across reconstruction algorithms: FBP and SAFIRE / J. Solomon, E. Samei // Medical Physics. – 2014. – Vol. 41, N 9. – P. 091908. DOI: 10.1118/1.4893497.

8. Sprawls P. The physical principles of medical imaging, 2nd Ed / P. Sprawls. – Madison, Wis.: Medical Physics Publishing, 1995. – 656 p.

#### PHANTOM WITH HETEROGENEOUS STRUCTURE OF METASTASES ON THE BASIS OF NANOCOMPLEX FOR COMPUTED TOMOGRAPH

#### V.E. Orel, A.V. Romanov, T.S. Golovko, G.V. Lavrik, N.A. Yoltukhovsky

Tissue-equivalent phantom of the liver with artificial metastases sizing  $\sim 5$  mm was developed. Metastases without nanoparticles were almost not visualized by computed tomography, in contrast to metastases with iron oxide nanoparticles, which were well visualized on the tomogram.

**Key words:** phantom, artificial metastases, liver, computed tomography.

#### ФАНТОМ З ГЕТЕРОГЕННОЮ СТРУКТУРОЮ МЕТАСТАЗІВ НА ОСНОВІ НАНОКОМПЛЕКСУ ДЛЯ КОМП'ЮТЕРНОГО ТОМОГРАФА

#### В.Е. Орел, А.В. Романов, Т.С. Головко, Г.В. Лаврик, М.О. Йолтуховський

Розроблено та виготовлено тканинно-еквівалентний фантом печінки з штучними метастазами розмірами ~5 мм. Метастази без наночастинок практично не візуалізувались методом комп'ютерної томографії, на відміну від метастазів з наночастинками оксиду заліза, які добре візуалізувались на томограмі.

*Ключові слова:* фантом, штучні метастази, печінка, комп'ютерна томографія.

#### ФАНТОМ С ГЕТЕРОГЕННОЙ СТРУКТУРОЙ МЕТАСТАЗОВ НА ОСНОВЕ НАНОКОМПЛЕКСА ДЛЯ КОМПЬЮТЕРНОГО ТОМОГРАФА

#### В.Э. Орел, А.В. Романов, Т.С. Головко, Г.В. Лаврик, Н.А. Йолтуховский

Разработан и изготовлен тканеэквивалентный фантом печени с искусственными метастазами размерами ~ 5 мм. Метастазы без наночастиц практически не визуализировались методом компьютерной томографии, в отличие от метастазов с наночастицами оксида железа, которые хорошо визуализировались на томограмме.

*Ключевые слова:* фантом, искусственные метастазы, печень, компьютерная томография.

#### Патенти

СПОСІБ ВЕРИФІКАЦІЇ МОЗОЧКОВОГО ДІАШИЗУ ПРИ ЧЕРЕПНО-МОЗКОВІЙ ТРАВМІ ІЗ ВИКОРИСТАННЯМ ОДНОФОТОННОЇ ЕМІСІЙНОЇ КОМП'ЮТЕРНОЇ ТОМОГРАФІЇ ТА МАГНІТНО- РЕЗОНАНСНОЇ ТОМОГРАФІЇ

120002; Каджая М.В., Макеєв С.С., Дядечко А.О., Новікова Т.Г., Готін О.С., Андрєєв О.А., Ніколов М.О., Коваль С.С.

Спосіб верифікації мозочкового діашизу при черепно-мозковій травмі із використанням однофотонної емісійної комп'ютерної томографії (ОФЕКТ) та магнітно-резонансної томографії (МРТ). Пацієнтам через 3-5 днів після отримання черепно-мозкової травми проводять (ОФЕКТ) з використанням Тс99m-ЕСD або 99mTc-HMPAO та МРТ, далі проводять ретроспективну інтеграцію отриманих томографічних зображень і за результатами порівняльної оцінки особливостей розподілу та нагромадження (Тс99m-ЕСD або 99mTc-HMPAO) та MP-контрастних речовин (контрастні речовини на основі гадолінію) уточнюють дані стосовно мозочкового діашизу при черепно-мозковій травмі.