Study of iodine, gadolinium and bismuth quantification possibility with micro-CT IVIS spectrumct in vivo imaging system

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Abstract. The main task of radiotherapy is to create prescribed absorbed dose of irradiation in a tumor with minimal damage of healthy tissues. Contrast Enhanced Radiotherapy allows to achieve that by administration of a special drug into the tumor before irradiation, that increases the absorbed dose within the tumor volume. The concentration of the drug determines the value of the absorbed dose, therefore one of the major tasks in CERT is quantification of the drug concentration in the tumor during irradiation procedure. The present work deals with quantitative determination of iodine, gadolinium and bismuth water solutions by use of micro-CT IVIS Spectrum In Vivo Imaging System.

1. Introduction

Therapy of malignant tumors is one of the most actual problems in modern medicine. Each of the conventional methods of treatment – surgical removal, chemotherapy or radiation therapy – has its own advantages and disadvantages. In particular in radiation therapy it is not always possible to create the necessary ratio of the absorbed dose value in tumor and normal tissues. The main goal of radiation therapy is to deliver tumoricidal value of absorbed dose into the tumor without exceeding the tolerant dose of healthy tissues surrounding the tumor.

One of the new methods in radiation therapy is Contrast Enhanced Radiotherapy (CERT). The method consists of tumor saturation with dose enhancing agent (DEA) following x-ray irradiation. DEA is any chemical element with atomic number $Z > 52$. The presence of DEA in the tumor leads to local increase of the absorbed dose caused by preferential external radiation photoabsorption by DEA atoms[1].

CERT allows to increase the value of the absorbed dose significantly within the irradiated target without exceeding tolerant dose in surrounding healthy tissue. Animal experiments have shown high efficacy of CERT in treatment of malignant tumors [2,3,4,5]. The value of the absorbed dose is determined by DEA concentration, so the determination of the DEA concentration in the tumor prior and during irradiation is one of the key issues arising in CERT implementation[6].

The aim of this work is to study the possibility of quantitative determination of iodine, gadolinium and bismuth by micro-CT IVIS Spectrum CT In Vivo Imaging System. Micro-CT IVIS is a widely used scientific instrument to study biodistribution of different substances labeled with fluorescent
dyes. The CT-function is a not primary function of this device, therefore the quality of the CT image is inferior to specialized preclinical micro-CT facilities. However, the wide distribution of this instrument and radiation safety allowing it’s installation in non-specialized rooms make the study of DEA quantification with micro-CT IVIS useful and practically significant for many research groups.

The following tasks were set to achieve the above mentioned goal:
1) Determine radiopacity of water in phantoms and air around them in arbitrary units of the micro-CT IVIS software using tomogram data obtained with IVIS.
2) Determine radiopacity of iodine, gadolinium and bismuth solutions with their different concentrations in microtubes inside a water phantom in arbitrary units of the micro-CT IVIS software using tomogram data obtained with IVIS.
3) Rescale obtained radiopacity data in arbitrary units to Hounsfield units considering water of 0 HU and air of -1000 HU.
4) Plot calibration curves for iodine, gadolinium and bismuth using rescaled data.

2. Materials and methods
The study was performed using micro-CT IVIS. Microtubes 250 ml containing different water solutions of iodine, gadolinium and bismuth were placed into 50 ml water filled cylinder with following dimensions 30х110 mm as visualized object. DEA concentration in microtubes was from 1 mg/ml to 50 mg/ml.

ImageJ software was used to measure the value of radiopacity in CT tomograms.

3. Results
Radiopacity of water along the longitudinal axis of the phantoms is shown in figure 1.

![Figure 1](image.jpg)

**Figure 1.** The dependence of water radiopacity values in arbitrary units (AU) on the distance from the tube cap along the longitudinal axis of the phantom.

The maximum change of AU value is observed in the center of the tube and is about 25%.

Because of the longitudinal AU value significant change, the dependence of Hounsfield units (HU) on AU was built for each slice (Fig. 2).
Using obtained calibration curves for each slice of phantoms the dependence diagrams of the radiopacity values of iodine, gadolinium and bismuth water solutions in the Hounsfield’s scale units on concentration of the elements were built (Fig. 3).

**Figure 2.** The example of a calibration curve.

**Figure 3.** The dependence of radiopacity in HU units on the concentration of iodine (♦), gadolinium (■) and bismuth (▲).

**Conclusion**

The comparison of the radiopacity data of iodine, gadolinium and bismuth water solutions in different concentrations has revealed:

1) almost the linear dependence of the radiopacity conventional units which determined according to the IVIS system data (and recalculated in Hounsfield units), solutions of I, Gd and Bi in the water phantom on the concentration of elements;

2) significant change of radiopacity of the same DEA concentration along the longitudinal axis of the phantom.
Thus, for the experimental quantification of DEA in the body of laboratory mice using IVIS, a correction of the signal along the longitudinal axis of the object is necessary, namely, for each tomographic slice.

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References
[1] J. C. Roeske, L. Nunez, M. Hoggarth et al. 2007 Technol. Cancer Res. Treat, 6(5), 395-401
[2] A. Norman, M. Ingram, R. G. Skillen et al. 1997, Radiat Oncol Investig, 5, 8–14
[3] J. F. Hainfeld, D. N. Slatkin, H. M. Smilowitz, 2004 Phys. Med. Biol., 49, N309–N315
[4] J. F. Hainfeld, H. M. Smilowitz, M. J. O’Connor et al. 2013, Nanomedicine, 8(10), 1601–1609
[5] Lipengolts A. A., Cherepanov A. A., Kulakov V. N., Grigorieva E. Y., Sheino I. N., Klimanov V. A. 2015. Antitumor efficacy of extracellular complexes with gadolinium in Binary Radiotherapy. Applied Radiation and Isotopes (2015)- Vol. 106.- Pp. 233-236
[6] V. N. Kulakov, A. A. Lipengol’ts, E. Yu. Grigor’eva, N. L. Shimanovskii. 2016. Pharmaceuticals for binary radiotherapy and their use for treatment of malignancies (a review). Pharmaceutical Chemistry Journal.-2016.- Vol. 50.- No. 6. Pp. 388-393