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The impact of iodinated contrast media on intravascular and extravascular absorbed doses in X-ray imaging: A microdosimetric analysis

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ABSTRACT

Studies suggest iodinated contrast media (ICM) may increase organ dose and blood cell DNA damage for a given X-ray exposure. The impact of ICM on dose/damage to extravascular cells and cancer risks is unclear.

Methods: We used Monte Carlo modelling to investigate the microscopic distribution of absorbed dose outside the lumen of arteries, capillaries and interstitial fluids containing blood and various concentrations of iodine. Models were irradiated with four X-ray spectra representing clinical procedures.

Results: For the artery model, The average dose enhancement factors (DEF) to blood were 1.70, 2.38, 7.38, and 12.34 for mass concentrations of iodine in blood ($\rho_i I$) of 5, 10, 50 and 100 mg/ml, respectively, compared to 0 mg/ml. Average DEFs were reduced to 1.26, 1.51, 3.48 and 5.56, respectively, in the first micrometre of the vessel wall, falling to 1.01, 1.02, 1.06 and 1.09 at 40–50 μm from the lumen edge. For the capillary models, DEF for extravascular tissues was on average 48% lower than DEF for the whole model, including capillaries. A similar situation was observed for the interstitial model, with DEF to the cell nucleus being 35% lower than DEF for the whole model.

Conclusions: While ICM may modify the absorbed doses from diagnostic X-ray examinations, the effect is smaller than suggested by assays of circulating blood cells or blood dose enhancement. Conversely, the potentially large increase in dose to the endothelium of blood vessels means that macroscopic organ doses may underestimate the risk of radiation induced cardiovascular disease for ICM-enhanced exposures.

1. Introduction

Iodinated contrast media (ICM) are frequently used in diagnostic X-ray imaging, including around 50% of CT scans [1], to improve visualization of blood vessels and other structures. In addition to well-known chemo/osmotoxic side effects, including allergic reactions and kidney damage [2], concerns have also been raised that contrast media may increase cancer risks from X-ray exposures [3,4]. Recently, we reviewed around four decades-worth of research investigating the radiation doses and associated DNA damage for ICM-enhanced, versus unenhanced X-ray exposures [5]. Increased DNA damage is likely to be a dosimetric effect, due to ICM molecules acting as a source of secondary radiation, i.e. photoelectrons, Auger electrons and photons. To date, all DNA damage assays have focused on cells in the blood itself, i.e. lymphocytes. While a clear suggestion of increased blood cell DNA damage for ICM-enhanced exposures was apparent (typically 30–100%, though up to 267%), it is unclear if these findings also imply an increased risk of developing cancer. In particular, it is not clear if the presence of iodine in blood vessels leads to DNA damage in extravascular cells, including those cells prone to malignant transformation.

Few studies investigating the dosimetric impact of ICM on tissues other than the blood in diagnostic X-ray imaging have been published [6–10]. These have generally focused on macroscopic doses, i.e. the mean absorbed dose to whole organs or phantoms, without assessing the microscopic pattern of energy deposition under ICM-enhanced conditions. As the dose perturbation effects of high Z elements are extremely close range (typically within a few tens of micrometres) [11], it may be possible for ICM to increase blood dose and macroscopic organ doses quite markedly with little impact on dose to cells outside blood vessels. To investigate this, and to help place blood cell DNA damage assays in context, we performed a microdosimetric analysis using the Monte Carlo code MCNP6.1 and three simple blood vessel models. The

Abbreviations: ICM, iodinated contrast media; DEF_{ICM}, Dose enhancement factor due to ICM

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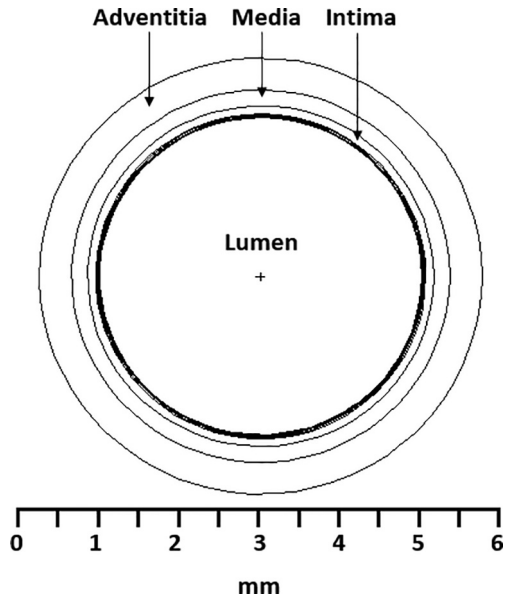

Fig. 1. Cross section of standard artery model. Length of artery is 5 cm. Build-up cylinder surrounding vessel not shown.

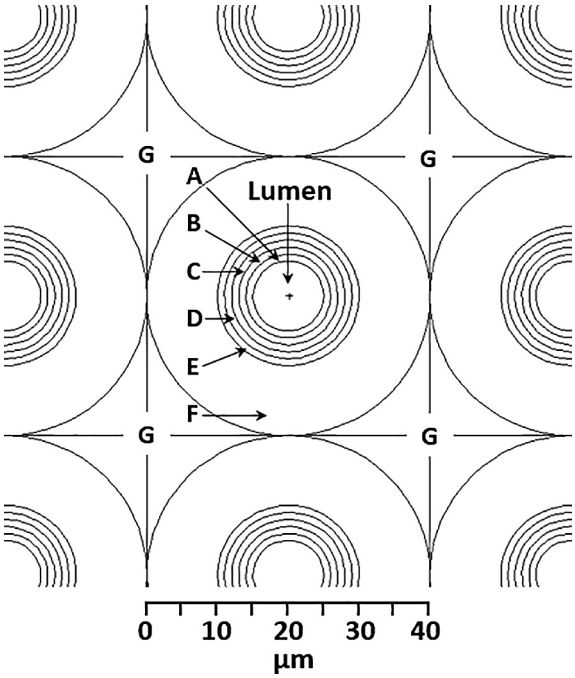

Fig. 2. Cross section of a portion of the model representing a network of capillaries in soft tissue. Labels A to G correspond to different regions in Table 3. Whole model is a 25 × 25 matrix of these elements, each 100 μm long.

aim of the study was to investigate ICM-associated enhancement of dose as a function of distance from the blood itself, for various concentrations of iodine in the blood and various beam spectra used in clinical X-ray imaging.

2. Methods

Three models were constructed. The first represented a single 5 cm long artery (Fig. 1) with radial dimensions typical of a coronary artery in a normal individual, based on previously published data [12–14]. The radius of the artery lumen was initially set at 2000 μm. The wall was divided into three anatomical layers, or 'tunicas', namely the intima (150 μm thick), media (200 μm) and adventitia (400 μm) [13], giving a total wall thickness of 750 μm [14]. To examine the dose distribution within the intima in detail, the first 10 μm of this layer was divided into concentric layers of 1 μm thickness. The innermost of these layers thus represented the single-cell-thick endothelium of blood vessels. The following 10 μm (i.e. 10–20 μm from the lumen edge) was divided into 2 μm layers and the next 30 μm (20–50 μm from the lumen edge) was divided into 10 μm layers.

Each layer of the vessel wall was composed of 'ICRP' 13-element soft tissue material (density, $\rho = 1.00\ g/cm^3$) obtained from the National Institute of Standards and Technology [15], except for the media, which was composed of ICRP muscle ($\rho = 1.04\ g/cm^3$). The lumen was filled with ICRP 13-element blood material ($\rho = 1.06\ g/cm^3$), combined with different mass concentrations of iodine ($\rho_I I$) (0, 5, 10, 50 and 100 mg I/ml). The density of the blood was adjusted to correspond to $\rho_I I$. The vessel was placed within a larger soft tissue cylinder of radius 10 cm to simulate electron build-up, scattering and beam hardening effects that would occur for vessels located deep within the body. A sensitivity analysis was performed by removing the build-up cylinder. Simulations were also repeated with different lumen radii (1000 and 4000 μm).

The second model represented multiple capillaries within a small block of soft tissue (Fig. 2). This was based around a 25 × 25 lattice of 40 × 40 × 100 μm cuboid elements, each containing a 'capillary' composed of ICRP blood material, of radius 5 μm and length 100 μm, surrounded by five concentric 1 μm thick layers of ICRP soft tissue (cells A–E in Fig. 2). The innermost of these layers was considered representative of the capillary wall. The extravascular remainder of each lattice element was also composed of ICRP soft tissue. As with the artery model, the lattice was placed within a soft tissue cylinder of radius 10 cm. The model was designed to represent a typical soft tissue with average capillary density. The distance between the edges of adjacent capillary lumens ranged from 30 μm to 47 μm. Blood made up 5% of the total volume of each lattice element.

A modified version of the capillary model was also produced, representing a more densely perfused tissue (Fig. 3). In this model, the lattice elements were reduced in size to 20 × 20 × 100 μm, while the capillaries were maintained at the same size. The distance between the edges of adjacent capillary lumens in the dense model ranged from 10 μm to 18 μm, with blood making up 20% of the volume of each lattice element. Sensitivity analyses were performed by adjusting the

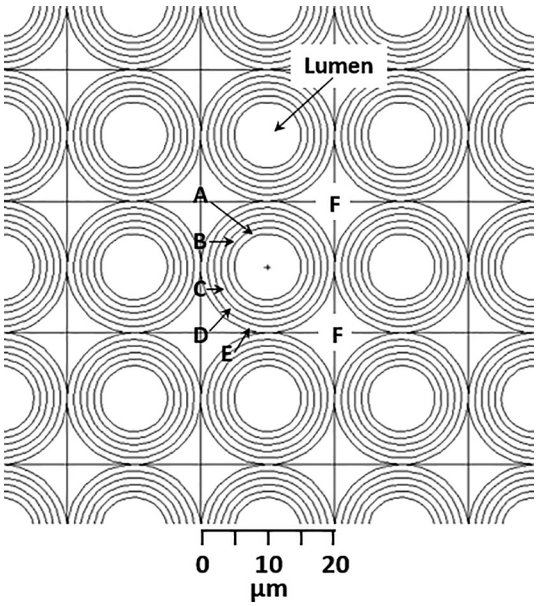

Fig. 3. Cross section of a portion of the dense capillary model. Labels A to F correspond to different regions in Table 4. Scale is the same as Fig. 2. As with Fig. 2, the whole model is a 25 × 25 matrix of elements, each 100 μm long.