Small-Scale Absorbed Dose Modelling in Selective Internal Radiation Therapy
Microsphere Distribution in Normal Liver Tissue

Akademisk avhandling

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av

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I. Högberg, J, Rizell, M, Hultborn, R, Svensson, J, Henrikson, O, Gjertsson, P, Bernhardt, P. Radiation exposure during liver surgery after treatment with ^{90}Y microspheres, evaluated with computer simulations and dosimeter measurements.
J. Radiol. Prot. 2012; 32: 439-446

II. Högberg, J, Rizell, M, Hultborn, R, Svensson, J, Henrikson, O, Mölne, J, Gjertsson, P, Bernhardt, P. Heterogeneity of microsphere distribution in resected liver and tumour tissue following selective intrahepatic radiotherapy.
EJNMMI Research 2014; 4:48

III. Högberg, J, Rizell, M, Hultborn, R, Svensson, J, Henrikson, O, Mölne, J, Gjertsson, P, Bernhardt, P. Increased absorbed liver dose in Selective Internal Radiation Therapy (SIRT) correlates with increased sphere-cluster frequency and absorbed dose inhomogeneity.
EJNMMI Physics 2015; 2:10

IV. Högberg, J, Rizell, M, Hultborn, R, Svensson, J, Henrikson, O, Mölne, J, Gjertsson, P, Bernhardt, P. A simulation model of microsphere distribution for selective internal radiation therapy agrees with observations.
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ABSTRACT

Radioembolisation (RE), with yttrium-90 (^{90}Y) labelled microspheres, is an increasingly common treatment method for unresectable liver tumours. The tolerable mean absorbed dose for normal liver (NL) tissue is higher in RE than in External Beam Radiation Therapy (EBRT); absorbed dose heterogeneity is thought to be one important reason, together with a low absorbed dose rate, but the knowledge of microsphere distributions is limited. The aim of this thesis was to describe macroscopic and small-scale heterogeneity in the distribution of microspheres and consequently in absorbed dose, and to create a hepatic branching artery tree model, able to reproduce normal liver microsphere and absorbed dose distributions. Another aim was to develop and evaluate a method for prediction of absorbed dose to the surgeon's hands during liver resection on still radioactive tissues.

Two patients with marginally resectable cholangiocarcinoma underwent resection, nine days after RE with resin SIR-Spheres®. Considering radiation safety, simulation of absorbed dose to surgeon's hands was performed with the software Varskin Mod 2® before surgery and absorbed dose rate measurements were done with thermoluminescent dosimeters (TLD) on resected tissue. The macroscopic sphere distribution within NL was investigated by gamma well chamber activity measurements on punch biopsies from sliced resected tissues and by calculating coefficient of variation (CV) and skewness (SK), in relation to biopsy mass. Small-scale heterogeneity in microsphere and absorbed dose distribution was studied by light microscopy and subsequent absorbed dose simulations by beta dose point kernel convolution. A branching artery tree model was used, to simulate microsphere and absorbed dose distributions.

Tissue measurements and simulations of absorbed dose to surgeon's hands showed similar results. The CV and SK of activity concentration, by gamma well chamber measurements, decreased rapidly with increasing mass and/or mean activity concentration. Aggregations of clusters increased in frequency and CV and SK for absorbed dose distribution increased with mean sphere concentration. The branching artery tree model was able to resemble the biopsy sphere and absorbed dose distributions.

Expected absorbed dose to the surgeon's hands was not alarming, but simulations and measurements of surgeon finger absorbed dose are recommended. Decreasing CV and SK for macroscopic distribution indicated a heterogeneous pattern larger than the punch biopsy masses investigated. Small-scale sphere and absorbed dose heterogeneity both increased with mean sphere concentration. The branching artery tree model helps to explain the distribution mechanism better than previous distribution models. The shown heterogeneity and the arterial tree model provide knowledge that may be helpful in optimising RE treatment, regarding number of injected spheres and activity per sphere.

Keywords: clusters, dosimetry, heterogeneity, liver, microspheres, radioembolisation, simulations, SIRT, surgery, yttrium-90