PhD Thesis Tittle: "Development of a three-dimensional dose calculation method in hepatic radioembolization treatment with yttrium-90 microspheres"

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ABSTRACT:

Hepatic radioembolization with ^{90}Y microspheres is a radiation therapy procedure during which little particles, loaded with this beta-emitter radioisotope, are implanted via the hepatic artery. Liver vascular anatomy and radiation characteristics allow the delivery of a high absorbed dose on tumor, with a low dose on healthy liver tissue, and a negligible level on surrounding organs. Dosimetry calculations are performed before treatment through the information of radiological and scintigraphic images. These are obtained after the administration of ^{99m}Tc-macroaggregated albumin during an angiographic procedure, analogous to the consequent real treatment.

The methodology used for dose calculations from radiopharmaceutical is the schema developed by the MIRD Committee. The application of this schema for radioembolization procedure is the so-called Partition Method, which uses the tumor-to-liver activity uptake ratio as the main parameter to obtain the mean dose in tumor and normal liver. Problems in tumor burden delimitation frequently prevent the use of the Partition Method. Even in the few cases where it can be applied, the method is poorly reproducible, because of the strong dependence on manual estimation of tumor-to-liver activity ratio from scintigraphic images. Other option is the use of three-dimensional dosimetry calculation methods. These offer more dosimetric information, providing the mean dose at the voxel level in scintigraphic images. Three-dimensional dosimetry is not so widely used, mainly due to complexity and also to the lack of available software in medical centers using this technique. At present, the target activity for radioembolization treatment is commonly obtained from non-personalized methods. Such dosimetric limitations imply a sub-optimal prescription, and prevent an improvement of dose-effects correlations, because of the impossibility of suitable absorbed dose quantification. The lack of personalized and standardized calculation tools and methodologies aggravates this situation, resulting in a deficient exchange of clinical information between professionals.

The first objective of this work was to present a modification of the Partition Method, through the estimation of the tumor-to-liver activity uptake obtained from the scintigraphy-derived numeric matrix. Segmentation of affected and normal parenchyma regions was obtained applying uptake thresholds to the gammagraphic study matrix. Thresholds were chosen by adjusting the resultant estimated volumes with the previous liver volumetry values. The second objective was to validate the proposed method, by comparison with a parallel dosimetry, accepted as a reference. The chosen reference

method was three-dimensional voxel dosimetry, based on a convolution between a dose deposition kernel and the time-integrated activity distribution derived from scintigraphy. Development of this three-dimensional method was an ancillary objective of this work. Both methods were developed using accessible tools: free software applications, software that is widely available in radiotherapy and nuclear medicine departments, and software developed for the purpose of this work using an open-source programming language.

Both methods were applied retrospectively to a sample of real patients treated with radioembolization. The obtained values for tumor-to-liver ratio, tumor mean dose and healthy liver mean dose were similar. The same parameters were estimated with the methods widely used in clinical practice, showing the differences. The influence of the proposed modification of the Partition Method in activity prescription was also evaluated. A good balance between simplicity, accuracy and reproducibility was obtained. Limitations on pre-therapy dosimetry caused by technical image characteristics were noted.

Both methods are a reliable option to calculate mean absorbed dose in tumor and normal liver. The proposed modification of the Partition method allows an estimation of dose from the whole activity distribution obtained in the scintigraphy. The process is fast and easily adaptable to other situations, like post-treatment dosimetry. Volumetry-based use of thresholds makes it very reproducible, and so partially reduces the inherent subjectivity of the Partition Method. It could improve the number of potential candidates for personalized dose calculation. The developed three-dimensional voxel dosimetry method is compatible with threshold segmentation or organ contouring over radiological images. It also offers spatial information, like dose distribution, dose-volume histograms and other dose parameters, besides mean dose.

References to author publications that relate specifically to the dissertation:

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2. F. Mañeru, A. Otal, M. Gracia, N. Gallardo, J. Olasolo, N. Fuentemilla, L. Bragado, M. Martin-Albina, S. Lozares, S. Pellejero, S. Miquelez, A. Rubio, "SU-E-T-02: 90Y Microspheres Dosimetry Calculation with Voxel-S-Value Method: A Simple Use in the Clinic," Med Phys 42, 3330 (2015).