## THESIS TOPIC

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**Personalized treatment for radioembolization of liver tumors: multi-scale vascular and dosimetric modeling**

**Unit / team:** LTSI, UMR 1099 INSERM, METRIQ

**Supervisor’s name:** ROLLAND Yan

**Phone number:** +33 2 99 25 30 00

**Email address:** y.rolland@rennes.unicancer.fr

**Socio-economic and scientific context (approximately 10 lines):**

Hepatocellular carcinoma (HCC) is the fifth most common malignant tumor, with more than 700,000 new cases a year worldwide [Giunchi17]. This is therefore a public health problem, especially since the treatment options for HCC are limited (15% surgery, 50% non-surgical treatment and 35% palliative treatment [Andreana12]). External radiotherapy has important contraindications because of the side effects of irradiation in surrounding tissues, and chemotherapy is limited by the development of resistance to treatment and many side effects as well.

$^{90}$Y radiolabeled microsphere internal radioembolization improves the targeting of the tumor and reduces toxicity. Although the anti-tumor action of this therapy has not yet been demonstrated [Ahmadzadehfar10] and [Salem13], recent studies have shown the need to take into account the dosimetry (dose delivered to the tumor) in the planning to improve still the efficiency and personalization of the treatment (response, survival).

**Working hypothesis and aims (approximately 8 lines):**

In addition to the interest of measuring the dose delivered to the tumor by the most innovative means (PET / CT), the estimation of it, upstream of the treatment (intraoperative phase) is a major issue. Macrovascular Sphere Distribution Modeling, initiated by LTSI researchers and CLCC physicians Eugène Marquis, should be continued at a more microscopic level and should be complemented by modeling the dose distribution in the tumor and tissues. healthy.

**Main milestones of the thesis (approximately 12 lines):**

The first objective of the thesis is to develop a microscopic model for the distribution of microspheres in the small vessels (hepatic arterioles) located at the level of the portal triads of a lobule (intra-lobule model) as well as of a set of lobules. This work can be based on preliminary studies proposed by [Walrand14]. The input data (blood flow, pressure, number of spheres) of this model will be assumed to be known at first, and must be representative of the physio-pathological state of the tissue (healthy, nodule, carcinoma). This model will have to make it possible to simulate the heterogeneity of the distribution (in particular the clusters of spheres), whose influence is great on the efficiency of the treatment [Högberg15].

The second objective of the thesis will be to develop a model of micro-dosimetry (based on existing models - Monte Carlo, Dose Point Kernel ...) to simulate the dose absorbed by tissues close to radioactive sources (microspheres), given a distribution of simulated spheres in the previous step. The effect of the inhomogeneity of the distribution (for the same quantity of microspheres) on the absorbed dose will be evaluated, thus making it possible to simulate an injection of the same number of activity via a a certain number of glass spheres, or a much larger number of resin spheres, reflecting the two characteristic cases applied in clinical routine.

The coupling of these models with a mesoscopic model of vessel growth, specific patient, already available at the LTSI should provide a 3D map of the dose absorbed by the tissues, and in particular by the tumor.

**Scientific and technical skills required by the candidate (2 lines):**

- Engineer or master with a degree in biomedical programming skills (C, C++, Matlab ...)
- Expertise in the field of image processing
- Basic knowledge in physics and mathematics
- Fluent English in writing and oral
- Working skills in close connection with multidisciplinary teams and / or with industrialists
- Analytical reasoning ability
- Competencies in the field of medical physics will be considered positively but are not mandatory.
- Knowledge in Computational Fluid Dynamics will be considered positively but is not mandatory.

**3 publications from the team related to the topic (last 5 years):**

### National and international collaborations:

- Politecnico Di Milano, Milan, Italy
- Technical University of Bialystok, Poland