A transport model for quantitative CEUS imaging of tumor perfusion

Jean-Michel Escoffre[2], Baudouin Denis de Senneville[1], Edward Oujagir[2], Ayache Bouakaz[2], Amélie Rébillard[3]

[1]UMR 1253, iBrain, Université de Tours, Inserm, Tours, France ; [2]UMR 5251 CNRS/University of Bordeaux/INRIA, Institut de Mathématiques de Bordeaux, Talence, France ; [3]Movement, Sport and Health Sciences Laboratory, University Rennes 2, ENS Rennes, Bruz, France.

Background, Motivation, and Objective

Using conventional histological techniques, Potiron *et al.,* reported that conventionally fractionated irradiation induced vascular maturation along with increased perfusion and decreased hypoxia [1]. These results imply that the vascular microenvironment plays a role in tumor reoxygenation. In the present study, we investigated the effects of radiotherapy on tumor perfusion in murine subcutaneous colorectal cancer model using contrast-enhanced ultrasound (CEUS). In addition, we introduced the use of a model based on a transport equation for the analysis of dynamic CEUS in oncology.

Statement of Contributions/methods

Mouse tumor model – Human prostate cancer cells PC3 were subcutaneously injected in nude mice. The tumors were treated or not (control) with radiotherapy (20 Gy, 4 fractions of 5 Gy) when the tumor volume reached 150 mm^3.

CEUS examination – A bolus of 70 uL of MM1 contrast agents was intravenously injected. Subsequently, CEUS video clip of 150 s was recorded to assess tumor perfusion.

CEUS analysis – As previously reported [2], physiological activity and motion of US probe were first compensated on the DCEUS images. Subsequently, the apparent microbubble transport was estimated using the transport equation (Figure). Tumor perfusion was also quantitatively analyzed using the existing TIC-based approach using VevoCQ software. The quantitative analyses of both approaches were compared.

Results/Discussion

The spatio-temporally averaged microbubble transport amplitude was significantly different ($p = 0.0286$) in the control group than in the radiotherapy group. In agreement with previous study [1], these results confirmed that radiotherapy increased the tumor perfusion, thus suggesting an improvement of the vasculature functionality after radiotherapy. Our proposed classification criterion has thus revealed to be better binary classification criterion for treated/control tumors than TIC-based parameters. None of these parameters led to a significant difference between both groups. Our methodology opens great perspectives for the clinical evaluation of tumor perfusion. Its validation on clinical CEUS images is on-going.

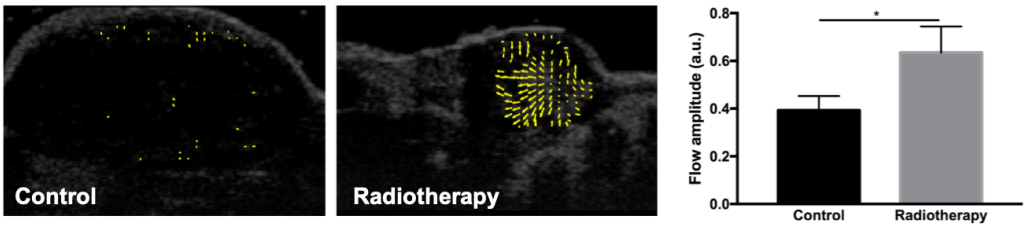

Figure legend: Assessment of tumor perfusion using the transport equation $I_t + \vec{V} \cdot \vec{\nabla} I = 0$ (I, grey level intensity on images; It, partial temporal derivative of I). The left part of this equation is composed by a transient term (It) and a transport term ($\vec{V} \cdot \vec{\nabla} I$), which stand for any temporal and spatial grey intensity variations, respectively.

[1] Potiron et al., PlosOne, 2013, 8:e84076.
[2] Denis de Senneville, et al., Trans. Med. Imaging, 2018, 37:372

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