Post-doctoral position

Combining Ultrasound and MRI biomarkers for early monitoring of cancer therapy and investigation of chemoresistance mechanisms

Location: CREATIS Laboratory (CNRS/INSERM/Université Lyon 1), based at Bâtiment Léonard de Vinci Campus La Doua, 21 avenue Jean Capelle, 69621 Villeurbanne, France.

Start date: Flexible, ideally end of 2026/beginning of 2027.

Funding: 2 years of funding from the INSERM PCSI project CUMBA. Net salary starting at 2428€, depending on experience.

Deadline: Applications will be reviewed on a rolling basis until the position is filled.

Context

Cancer is the leading cause of death in France, and early detection is crucial for improving survival. Early imaging-based assessment of treatment efficacy—through markers such as cell death or tumor modification—would enable rapid confirmation of therapeutic response and, in non-responding tumors, allow timely adjustment of therapy without waiting for postoperative pathological evaluation, as often occurs with bone sarcomas.

Quantitative ultrasound (QUS) parameters derived from ultrasound measurements of the backscatter coefficient (BSC) have been shown to be useful for monitoring anti-cancer therapies that induce apoptosis or mitotic catastrophe, for example [1,2]. In particular, these parameters have been used to show whether or not preclinical or clinical breast cancer tumors are responding to therapy [3]. **Ultrasound parameters derived from BSC and envelope statistics are related to tissue microstructure** [4] and may therefore be of interest for assessing necrosis or morphological changes of the tissue due to the therapy as an efficacy criterion of conventional therapy or for evaluating new therapies that affect tumors microstructure differently. In a previous study [5], we highlighted changes in ultrasound parameters on osteosarcoma were associated with changes in chromatin and collagen condensation in tumors that ultimately showed unresponsive to therapy.

MRI imaging, as **diffusion-weighted MRI (DW-MRI) is sensitive to macromolecular and microstructural changes** which can occur at the cellular level even earlier than anatomical changes during therapy. DWI-MRI provides the apparent diffusion coefficient (ADC) that measures water diffusion and tends to decrease in tissues with high cellularity. This technique shows promise for evaluating cancer treatment response via the quantification of ADC values [6–8]. **Magnetic resonance elastography** (MRE) is a noninvasive technique that **quantifies tissue biomechanical properties**. Tissue stiffness undergoes significant changes during the development and progression of cancer, and MRE has been used to detect and characterize malignant tissue, assess treatment response and explore the underlying tissue biomechanics of tumors [9,10].

Osteosarcomas are particularly resistant to conventional treatments. Despite aggressive therapeutic protocols, combining surgery and chemotherapy, the 5-year survival rate for patients with metastatic or relapsed osteosarcoma remains below 30%. Recent advances in immunotherapy have shown promise in their treatment. For instance, **immunomodulatory approach can induce significant changes in the tumor microenvironment** that can disrupt the tumor's immune evasion mechanisms, creating an environment more conducive to therapeutic efficacy [11]. The osteosarcoma model

provides a particularly robust framework for validating our imaging-based approach. Its exceptionally high rate of therapeutic resistance (60–70% non-responders) makes it an ideal stress test—if imaging biomarkers prove effective here, they are likely to be applicable to more responsive tumors. Osteosarcoma also offers a clear and standardized pathological reference for treatment response (Huvos grade), enabling strong ground-truth validation. In addition, its highly heterogeneous microenvironment, located at the bone–soft-tissue interface, creates a particularly challenging environment for imaging-based analyses. The mechanisms of resistance are well characterized and relevant to other sarcomas, further reinforcing the model's translational value. Finally, established murine models such as MOS-J provide reliable and reproducible tumor growth patterns, ensuring experimental consistency.

Therefore, the central hypothesis in the CUMBA project is that cancer therapy triggers a cascade of biological changes that manifest as measurable physical properties (illustrated in Figure 1 (left panel)). Treatment-induced cell death decreases tissue cellularity, reducing both acoustic impedance (US-detectable) and tissue stiffness (MRE-measurable). Simultaneously, extracellular matrix degradation alters collagen architecture, modifying backscatter coefficient. Immune infiltration and vascular remodeling create spatial heterogeneity potentially detectable across all modalities. **We propose that ultrasound spectroscopy and multiparametric MRI provide complementary windows into this biological remodeling:** US parameters (BSC, Nakagami parametres) reflect microscopic tissue organization (cell size, nuclear condensation), while MRI captures tissue-scale properties (stiffness via MRE and diffusion and perfusion via DW MRI). This multimodal signature will be more sensitive than individual parameters because each modality probes different aspects of the same underlying biological response, creating a comprehensive picture of treatment efficacy detectable before tumor shrinkage. **The innovation lies in mechanistically linking these physical measurements to resistance pathways:** early non-responders will show distinct imaging patterns corresponding to specific molecular signatures (identified through RNA-Seq), enabling predictive biomarker development.

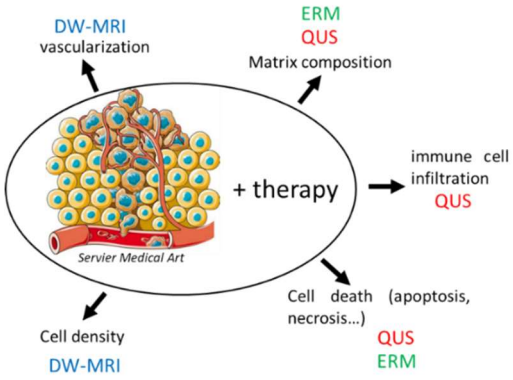

Figure 1: Potential therapy-induced changes in tumors and the imaging modality proposed in this project that could enable their detection.

Postdoctoral Position Objective

We propose a 2-year postdoctoral position focused on ultrasound and MRI acquisition and post-processing, as well as investigating the relationship between imaging and biological parameters.

The postdoctoral fellow will work on the design and improvement of the ultrasound and MRI imaging acquisition setup. An initial study enabled MRI diffusion, ERM, and ultrasound measurements on osteosarcoma tumors but requires improvements, notably the implementation of a higher-frequency ERM setup, in vivo ultrasound attenuation measurements, and multi-frequency ultrasound measurements.

The postdoctoral fellow will be involved in ultrasound and MRI acquisition campaigns involving various treatments—including chemotherapy and immunomodulation—on both chemotherapy-resistant and non-chemotherapy-resistant tumors. He or she will perform post-processing to estimate BSC-derived parameters and envelope statistics, diffusion maps, and ERM maps. He or she will also investigate the correlation between imaging parameters and histological and molecular imaging analyses (RNA sequencing).

Supervision

The post-doc will be supervised by Pauline Muleki Seya (Ultrasound imaging team) and Pilar Sango Solanas (MRI team) in collaboration with Aurélie Dutour (Cancer Research Center in Lyon). Ultrasound and MRI acquisitions will be realized in CREATIS PILoT platform on mice.

Candidate profile

The candidate should ideally hold a degree in engineering, or equivalent, with a specialization in biomedical imaging, particulary in ultrasound and/or MRI acquisition and signal processing. The candidate must be able to work independently and have knowledge of MATLAB programming and signal/image processing. Experience or skills in medical applications are appreciated. **Please note that this postdoctoral position will involve a significant amount of experimental work, including animal experiments on mice.**

Application

To apply, please send by e-mail a cover letter highlighting your motivation and fit for the project, your CV (including publications, technical skills, and references) and contact information for 2–3 references (including PhD supervisor) to pauline.muleki-seya@creatis.insa-lyon.fr and pilar.sango@creatis.univ-lyon1.fr.

Bibliography:

[1] Kolios MC, Czarnota GJ, Lee M, Hunt JW, Sherar MD. Ultrasonic spectral parameter characterization of apoptosis. Ultrasound in Medicine & Biology 2002;28:589–97. https://doi.org/10.1016/S0301-5629(02)00492-1.
[2] Vlad RM, Alajez NM, Giles A, Kolios MC, Czarnota GJ. Quantitative Ultrasound Characterization of Cancer Radiotherapy Effects In Vitro. International Journal of Radiation Oncology*Biology*Physics 2008;72:1236–43. https://doi.org/10.1016/j.ijrobp.2008.07.027.
[3] Sadeghi-Naini A, Sannachi L, Pritchard K, Trudeau M, Gandhi S, Wright FC, et al. Early prediction of therapy responses and outcomes in breast cancer patients using quantitative ultrasound spectral texture. Oncotarget 2014;5:3497–511.
[4] Oelze ML, Mamou J. Review of Quantitative Ultrasound: Envelope Statistics and Backscatter Coefficient Imaging and Contributions to Diagnostic Ultrasound. IEEE Transactions on Ultrasonics, Ferroelectrics, and Frequency Control 2016;63:336–51. https://doi.org/10.1109/TUFFC.2015.2513958.
[5] Malinet C, Mansilla C, Fajnorova I, Ducrot C, Rohfritsch A, Melodelima D, et al. Evaluation of Chemotherapy Response in Osteosarcoma Using Quantitative Ultrasound: A Pilot Study Relating Ultrasound Parameters to Molecular Response. IRBM 2025;46:100914. https://doi.org/10.1016/j.irbm.2025.100914.
[6] Mesny E, Leporq B, Chapet O, Beuf O. Intravoxel incoherent motion magnetic resonance imaging to assess early tumor response to radiation therapy: Review and future directions. Magnetic Resonance Imaging 2024;108:129–37. https://doi.org/10.1016/j.mri.2024.02.008.
[7] Kubo T, Furuta T, Johan MP, Ochi M, Adachi N. Value of diffusion-weighted imaging for evaluating chemotherapy response in osteosarcoma: A meta-analysis. Molecular and Clinical Oncology 2017;7:88–92. https://doi.org/10.3892/mco.2017.1273.
[8] Asmar K, Saade C, Salman R, Saab R, Khoury NJ, Abboud M, et al. The value of diffusion weighted imaging and apparent diffusion coefficient in primary Osteogenic and Ewing sarcomas for the

monitoring of response to treatment: Initial experience. European Journal of Radiology 2020;124:108855. https://doi.org/10.1016/j.ejrad.2020.108855.

[9] Pepin KM, Ehman RL, McGee KP. Magnetic resonance elastography (MRE) in cancer: Technique, analysis, and applications. Progress in Nuclear Magnetic Resonance Spectroscopy 2015;0:32. https://doi.org/10.1016/j.pnmrs.2015.06.001.

[10] Pepin K, Grimm R, Kargar S, Howe BM, Fritchie K, Frick M, et al. Soft tissue sarcoma stiffness and perfusion evaluation by MRE and DCE-MRI for radiation therapy response assessment: a technical feasibility study. Biomed Phys Eng Express 2019;5:047003. https://doi.org/10.1088/2057-1976/ab2175.

[11] Yu S, Yao X. Advances on immunotherapy for osteosarcoma. Mol Cancer 2024;23:192. https://doi.org/10.1186/s12943-024-02105-9.