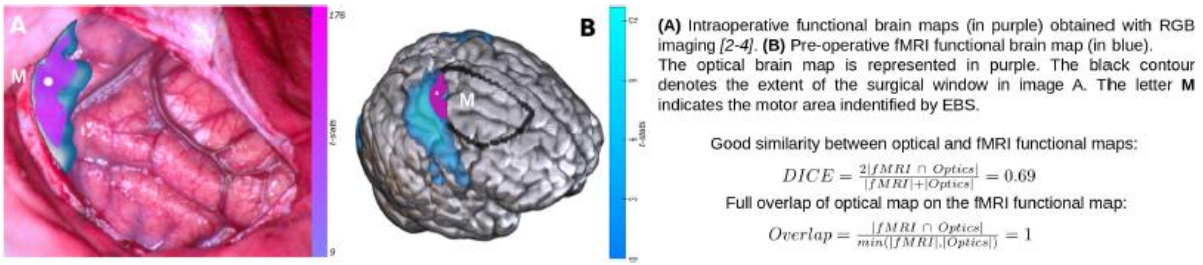
Intraoperative multimodal Optical/US imaging of hemodynamics for neurosurgery guidance

Context:
The impact of medical imaging is important for the early diagnostic and for the intervention guidance on pathologies. There is a growing interest for robust intraoperative techniques. Medical imaging clinical standards (MRI, nuclear medicine, CT…) face limitations in the operative room, due to technical, cost and regulatory constraints. Moreover, intraoperative imaging should be real-time to prevent any obstruction in the course of the surgery. Ultrasound and optical medical devices are relevant in this intraoperative context because they are easy to handle, reliable, generally low-cost, and allow high acquisition rate. Optics also have the huge advantage of being a non-contact imaging modality and to be close to the current practice in neurosurgery (surgical microscopes is a clinical standard in surgery). However, the diffusion of intraoperative optical devices is still limited because of a lack of reliable intraoperative biomarkers [*Morone et al. 2017*].
Hemodynamics is the cornerstone biomarker of numerous applications, particularly in intraoperative neuroimaging.; like identification of functional brain areas during intracerebral surgical procedures [*Caredda et al. 2019*] as shown on figure, tissue perfusion investigation for cancer imaging [*Berhouma et al. 2020*] or vascular pathologies. Hemodynamics can be assessed by spectral optical or US means, but both suffers from limitations. Indeed, optical methods are very sensitive to molecular contrast and are able to evaluate molecular concentrations of hemodynamics compounds (Oxy- and deoxy-hemoglobin) [*Caredda et al. 2020*], but lack sensitivity to flux properties. On the other hands, US methods are very sensitive to mechanical properties and can follow hemodynamics flux [*Deffieux et al. 2021*]. Furthermore, optical means are intrinsically limited to surface imaging due to light scattering in tissues, whereas US can assess flux in depth. Then, combining intraoperative optical and US modalities will allow a robust monitoring of the complex molecular/mechanical contrasts of hemodynamics.



(A) Intraoperative functional brain maps (in purple) obtained with RGB imaging *[2-4]*. **(B)** Pre-operative fMRI functional brain map (in blue). The optical brain map is represented in purple. The black contour denotes the extent of the surgical window in image A. The letter **M** indicates the motor area indentified by EBS.

Spectral optical imaging techniques range from standard 3-colors camera (RGB) to more specialized hyperspectral camera. Hemodynamic is directly linked to oxy-hemoglobin (HbO2), deoxy-hemoglobin (Hb), and cytochrome-c-oxidase concentration variations, which are the main chromophores in tissues. Monitoring of brain surface hemodynamic by optical camera consists in unmixing these concentration variations from the measurement of the optical intensity variation at different wavelengths. Temporal analyses of these biomarkers provide micro and macroscopic indications of brain activation. In preclinical studies with mouse models, quantification of these biomarkers allows the study of neurovascular coupling [*Montgomery et al 2020; Ma, Y. et al. 2016*].

The complementary of tissue hemoglobin perfusion and flux was investigated using laser speckle and spectral optical imaging [*Seong M et al. 2016; Steimers et al 2013*]. These works showed that laser speckle imaging highlights the spatial microvascularization at higher resolution than spectral imaging while the spectral imaging provides coarser resolution with more quantitative analysis. However, laser speckle has the same limitation, intrinsic to optical means, to surface imaging.

Functional ultrasound imaging is a novel ultrasound imaging technique able to identify regions of the brain involved in specific cognitive activities thanks to ultra-sensitive power Doppler imaging. This

breakthrough relies on the same principle as optical or MR functional imaging, i.e. the neurovascular coupling. Is has become possible with the emergence of ultra-fast ultrasound imaging and has even led to micro-vascularization imaging thanks to ultrasound localization microscopy which is possible when contrast agent is injected. As demonstrated by several groups it is now possible to perform such imaging in three dimensions (3D) but the challenges are still important. Real-time processing of the huge amount of data or imaging through the skull bone are two examples of such challenges.

Work directions:
We will explore the complementarities of tissue hemoglobin perfusion and flux using bimodality optical/US approaches. This coupling will allow to go further the intrinsic limitation of optical means to surface imaging and then to 2D flux (parallels to the brain surface). We will have access to 3D dynamics (adding the direction of depth), this could impact the fine understanding of neuronal mechanisms underlying brain hemodynamics and open new contrasts directions. We will also investigate the link between blood flux and perfusion (blood volume). This is also essential to understand the underlying parameters of the brain hemodynamic response induced by cerebral activity [*Buxton R. et al. 2004*] and retrieve the more local tissue oxygen extraction parameters. We will apply model extrapolated from combination of coherent imaging like laser speckle and spectral optical imaging to obtain local tissue oxygen extraction parameters [*Verdecchia K, et al 2013*].

Profile: student with a masters degree or an engineering degree, with background in wave physics or more simply optical and/or ultrasound imaging. Skills in signal/image processing and programming will be necessary. The project will necessitate to perform acquisitions and experimentations. The candidate should be willing to perform such experimental work including small animal imaging.

Applications: send CV – transcripts of the grades obtained during the last two years - contact of potential professor who could recommend you. All this should be sent to liebgott@creatis.insa-lyon.fr, montcel@creatis.insa-lyon.fr, pauline.muleki-seya@creatis.insa-lyon.fr, caredda@creatis.insa-lyon.fr .

References :

Morone K. A., et al., Neurophoton. 4(3), 031220 (2017)
Caredda C., et al. Neurophotonics , 6(4) :1 # 14, 2019. DOI: 10.1117/1.NPh.6.4.045015
Caredda C et al., Applied Sciences 2020, 10, 5158 DOI:10.3390/app10155158
Deffieux T. et al., Neuroscience 474 (2021) 110–121
Ma, Y.; et al. Proc. Natl. Acad. Sci. USA 2016, 113, E8463–E8471. DOI: 10.1073/pnas.1525369113
Montgomery et al. Cell Rep. 2020, 31, 107500. DOI: 10.1016/j.celrep.2020.03.064
Seong M, et al. J Biomed Opt. 2016 Feb;21(2):27001. doi: 10.1117/1.JBO.21.2.027001
Steimers et al. Adv Exp Med Biol; 789:427-433; 2013 DOI: 10.1007/978-1-4614-7411-1_57
Buxton R. ; et al. Neuroimage 2004;23 Suppl 1:S220-33. DOI : 10.1016/j.neuroimage.2004.07.013
Verdecchia K, et al. J Biomed Opt. 2013 Feb;18(2):27007. doi: 10.1117/1.JBO.18.2.027007
Berhouma M, et al. Neurooncol Adv. 2020 Aug 27;2(1). doi:10.1093/noajnl/vdaa108