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## PhD Thesis subject – Version Feb. 2025

Laboratory : Institut Fresnel, UMR 7249 CNRS/Centrale Méditerranée/Aix-Marseille Univ

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Partnership: Institut Fresnel / Hôpital Européen Marseille / Amidex foundation

Thesis title: **Laser Speckle Contrast Imaging for surgical assistance in thyroid surgery**

### Description of the thesis subject :

In line with an AMidex-funded collaborative project (see below) between two research teams at Institut Fresnel (DiMABio and Phyti) and Hôpital Européen (Marseille's site, Dr. F. Benmiloud), the aim of this PhD thesis is to develop an advanced methodology and laser imaging device based on speckle contrast analysis [1-3], to highlight the vascularization of parathyroid glands during thyroidectomy, and thus assist the surgical procedure in real time and without labelling. In this very common procedure (35,000/year in France), a major challenge is to preserve the integrity of the parathyroid vascular network (which is difficult to see despite the surgeon's trained eye), or risk disabling side-effects for patients, the incidence of which can be high [4]. The vascular imaging technique currently used in the OR is fluorescence imaging, which has a number of drawbacks (injection of a bolus of fluorescent dyes that dissipate rapidly (~4 min) throughout the vascular network, diffusion of biological tissues, etc.).

Relying on the expertise of research teams in speckle imaging [5-7], diffuse optical imaging in tissues [8,9], high-speed statistical image processing [10,11] and on the surgeon's own imaging practice [13-15], the thesis scientific project will focus on the development of the imaging chain (illumination and image capture device, image processing algorithms and display), which must be designed to be real-time, ergonomic and sterilizable for rapid use in the operating room, with the aim of obtaining preliminary test results in the operating room. A comparative study will also be carried out with the methods used routinely (autofluorescence imaging and indocyanine green angiography), which have disadvantages (need for marking in ICG angiography) that the project intends to address.

In addition, new scientific paths are to be explored in the PhD, including :

- optimization of real-time image processing and blood-flow/vascularity automatic segmentation, relying on the skills of the Phyti team in real-time statistical image processing [10-12], and in particular on unsupervised segmentation algorithms that can be well suited to the context of speckle contrast images [12].
- exploring the ability to provide quantitative imaging (blood flow velocity, possibly tissue oximetry, etc.) using two-wavelength illumination for instance, and using the strong know-how of the DiMABio team in quantitative diffuse optical imaging methods [8,9].
- assessing the interest of polarimetric sectioning in this context of correlation speckle imaging [8,9], which can prove useful in order to gain some insight on the 3D organization of the vascularities around the parathyroid glands.

## **Public summary of the collaborative scientific project :**

Within an emerging partnership between two research teams at the Institut Fresnel and the Hôpital Européen (Marseille site), the collaborative project AMidex SPECIALTHY (*SPEckle Contrast Imaging in reAL-time for safer THYroid surgery*) [Sept. 2024-Aug. 2025] aims at developing a laser imaging methodology and device based on speckle contrast analysis, to highlight the vascularization of parathyroid glands during thyroidectomy, and thus assist the surgical procedure in real time and in a label-free manner. In this very common procedure (35,000/year in France), a major challenge is to preserve the integrity of the parathyroid vascular network (difficult to see despite the surgeon's trained eye), which, if damaged may lead to disabling side-effects for patients, the incidence of which can be high. The imaging chain (illumination and image capture device, image processing algorithms and display) will have to be designed to be real-time, ergonomic and sterilizable for use within a short time frame in the operating room, with the aim of obtaining preliminary clinical results by the end of this 1-year project. A comparative study will also be carried out with routine methods (autofluorescence imaging and indocyanine green angiography), which have drawbacks that the project intends to address (need for labelling for ICG angiography). Among the scientific paths to be explored in the project, optimization of real-time image processing and the ability to provide quantitative imaging (blood flow velocity, possibly tissue oximetry, etc.) will be the main topics of innovation sought.

## **References :**

- [1] Mannoh, E.A., Thomas, G., Solórzano, C.C. et al. Intraoperative Assessment of Parathyroid Viability using Laser Speckle Contrast Imaging. *Sci Rep* 7, 14798 (2017).
- [2] Mannoh, E.A., Baregamian, N., Thomas, G. et al. Comparing laser speckle contrast imaging and indocyanine green angiography for assessment of parathyroid perfusion. *Sci Rep* 13, 17270 (2023).
- [3] Mannoh, E.A.; Thomas, G.; Baregamian, N.; Rohde, S.L.; Solórzano, C.C.; Mahadevan-Jansen, A. Assessing Intraoperative Laser Speckle Contrast Imaging of Parathyroid Glands in Relation to Total Thyroidectomy Patient Outcomes. *Thyroid*, 31, 1558–1565.3589 (2021).
- [4] Mathonnet M, Cuerq A, Tresallet C, Thalabard J-C, Fery-Lemonnier E, Russ G, et al. What is the care pathway of patients who undergo thyroid surgery in France and its potential pitfalls ? A national cohort. *BMJ Open* 2017;7:e013589 (2017).
- [5] **J. Fade** and M. Alouini, "Depolarization Sensing by Orthogonality Breaking", *Phys. Rev. Lett.*, 109, 043901 (2012).
- [6] **Fade J., Roche M.**, Alouini M., « Computational polarization imaging from a single speckle image », *Optics Letters*, 37, (3), 386–388 (2012)
- [7] Alesya Mikhailovskaya, **Julien Fade**, Jérôme Crassous. "Probing nonaffine expansion with light scattering". *Physical Review E*, 104 (5), pp.055004 (2021).
- [8] Susmita Sridhar and **Anabela Da Silva**, "Enhanced contrast and depth resolution in polarization imaging using elliptically polarized light," *J. Biomed. Opt.* 21(7), 071107 (2016).
- [9] Ugo Tricoli, Callum M. Macdonald, Turgut Durduran, **Anabela Da Silva**, and Vadim A. Markel, "Diffuse correlation tomography in the transport regime: A theoretical study of sensitivity to Brownian motion," *Phys. Rev. E* 97(2), 022408, (2018).
- [10] F. Galland, **N. Bertaux** and Ph. Réfrégier, Multicomponent image segmentation in homogeneous regions by stochastic complexity minimization, in *Pattern Recognition*, Vol. 38(11), pp. 1926–1936, (2005).
- [11] Mailfert S., Touvier J., Benyoussef L., Fabre R., Rabaoui A. Blache, M.C., Hamon, Y., Brustlein S., Monneret S., Marguet D. and **Bertaux N.**, A Theoretical High-Density Nanoscopy Study Leads to the Design of UNLOC, a Parameter-free Algorithm, *Biophysical Journal*, 115 (3), 565–576, (2018).
- [12] **J. Fade, M. Roche**, F. Galland, P. Réfrégier. Estimation of the degree of polarization from a single image: characterization of the precision under various coherent imaging conditions. *OPTO/IRS<sup>2</sup> Conference*, May 2008, Nürnberg, Germany.
- [13] **Benmiloud F**, Godiris-Petit G, Gras R, et al. Association of Autofluorescence-Based Detection of the Parathyroid Glands During Total Thyroidectomy With Postoperative Hypocalcemia Risk: Results of the PARAFLUO Multicenter Randomized Clinical Trial. *JAMA Surg.*, 155(2):106–112 (2020).
- [14] **Benmiloud, F.** et al. "Impact of autofluorescence-based identification of parathyroids during total thyroidectomy on postoperative hypocalcemia: a before and after controlled study." *Surgery* 163.1, 23–30 (2018).
- [15] Karcioglu, Amanda L. Silver, et **Benmiloud F.** et al. "Emerging imaging technologies for parathyroid gland identification and vascular assessment in thyroid surgery: A review from the American head and neck society endocrine surgery section." *JAMA Otolaryngology-Head & Neck Surgery* (2023).