ANNOUNCEMENT OF A PhD THESIS POSITION

In the framework of their joint research federation (Fédération Claude Lalanne), Université Côte d'Azur (Institute of Physics of Nice, CNRS UMR 7010) and the Centre Antoine Lacassagne (anti-cancer institute of Nice), invite applications for a PhD thesis on the topic below. The position will be based in Nice (Faculty of Sciences and Centre Antoine Lacassagne), France.

Contribution to the Development of Fiber-Based In-Vivo Realtime Dosimeters for Pulsed Radiotherapy

General context

This PhD thesis is proposed in the framework of the FIDELIO project ("Fiber-based In-Vivo Realtime Dosimeters for pulsed Radiotherapy", Feb. 2021- Jan. 2025), led by Université Côte d'Azur (Fédération Claude Lalanne, Institute of Physics of Nice and Centre Antoine Lacassagne). This project has been selected and funded following the 2020 call for proposals by the French National Research Agency (ANR). FIDELIO is a collaborative research program which also involves other academic and industrial partners: University of Lille (PhLAM – Physics, Lasers Atoms and Molecules laboratory – CNRS UMR 8523), France, Université Jean Monnet (LabHC – Laboratoire Hubert Curien – CNRS UMR 5516), Saint-Étienne, France, and the iXblue Company (Photonics division, Specialty fibers and components department, Lannion, France), a world-recognized leading player in the development of novel specialty optical fibers and fiber sensors.

Radiotherapy (RT) is included in more than one half of therapeutic managements of the ~400,000 new cancer cases diagnosed each year in France. The efficacy and safety of RT treatments require planning and checking accurately the radiation doses delivered to patients. Dosimetry is used to ensure quality assurance (QA) of accelerators, patient plans and treatments (in-vivo dosimetry, IVD). RT techniques have been significantly improved for 20 years. Refinements have constantly aimed at a much better conformation of the dose deposition to the tumor, and hence at a better sparing of the surrounding healthy tissue. Increasingly advanced variants of the so-called Intensity-Modulated RT (IMRT) have been developed from the early 2000s. They have been supplemented by stereotactic RT techniques, where an increased number of 'micro-beams' allow treating small tumors with a high precision level. Dose shaping can also be optimized thanks to improved tumor tracking, as now permitted by magnetic resonance imaging-guided RT (MRI-guided RT).

Typical size of the sensitive volume of state-of-the-art radio-electric dosimeters (1-3 mm) has become too large to resolve the high dose gradients inherent in highly conformational irradiation fields. Because of their even larger outer dimensions, these dosimeters may also impair the dose delivery when used for IVD in miniaturized fields. Radio-electric sensors are moreover not compliant with the electromagnetic environment of MRI-guided RT. Further major problems are raised by RT techniques using pulsed beams, as high-energy proton-therapy (HEPT) and flash-RT. HEPT is an effective technique to treat deep-seated tumors, firstly directed at pediatric indications owing to its outstanding preciseness. Its current technology is based on superconducting synchrocyclotrons (S2C2) delivering protons up to 226 MeV within pulses < 8 µs (repeated at 1 kHz) and beam spots of a few millimeters in diameter (pencil beam scanning). The peak dose rate is then about 4-10 Gy s^{-1}, ~100 times above that of conventional RT (0.01 – 0.07 Gy s^{-1}). Flash-RT consists in delivering high per-fraction doses with short irradiation pulses (< 500 ms) but high dose rate > 40 Gy s^{-1} (>1000 times that of conventional RT). Although at a pre-clinical assessment stage, flash-RT is considered the main breakthrough of the next few years because it seems to elicit significantly less side effects at constant therapeutic benefit. The problem is that such high dose rates are close to the limit of (or out of) the specifications of current radio-electric dosimeters.

There is therefore an urgent need in innovative real-time dosimeters that should be: (*i*) miniaturized, to greatly improve spatial resolution and for not hampering the dose delivery when used for IVD; (*ii*) designed to measure high dose rates (at least 50 Gy s^{-1}) and short pulses (down to 10 µs); (*iii*) immune to electromagnetic fields, to allow operation in MRI-guided RT. (*iv*) In the case of proton dosimetry, their response should be as insensitive as possible to the linear energy transfer (LET), so as not to impair the measurement of their depth-dose profiles. Usual qualities are also expected: the response should be proportional to the probed dosimetric quantity, with a stable and repeatable coefficient. Its dependence on extrinsic parameters (humidity, pressure, temperature, beam angulation) and on beam energy should be weak. The FIDELIO project proposes to develop such new sensors and to validate their use in relevant clinical conditions. The need for high dose-rate operation obviously excludes making new dosimeters work on a radio-electric conversion principle. The metrology will rather be based on radio-optical conversion (scintillation) via the **radioluminescence (RL)** phenomenon. RL probes will take the form of thin (< 0.5 mm) and short (< 1 cm) **silica-based optical fibers**.

Thesis work

The Institute of Physics of Nice (INPHYNI) and the Centre Antoine Lacassagne (CAL) are globally in charge of two complementary activities along the project. The first, led by INPHYNI, is related to the understanding of the basic RL processes in the silica-based RL probes produced by the Lille (PhLAM) and Lannion (iXBlue) partners, for both photons and protons. This notably relies on a significant amount of laboratory experimental work (pre-clinical assessment and screening of the possible probes), but also includes modelling aspects to issue recommendations and routes for improving the RL kinetics and sensitivity (manufacturing orientation). The second crucial contribution, led by CAL, is about the assessment and the validation of the RL dosimeters at the clinical level. This will again include a large amount of measurements and tests using the CAL medical accelerators, including the CyberKnife® (stereotactic, photon RT), the MEDICYC cyclotron (65 MeV, low-energy protontherapy) and the ProteusOne® synchrocyclotron (226 MeV, high-energy protontherapy). This experimental work is aimed at assessing the performance of the fiber probes throughout the optimization process (with feedback towards design and fabrication). At the end of this process, it will serve for the clinical validation of the final probes, against reference data gained from gold-standard dosimeters and Monte-Carlo simulations (through, e.g., profiles and percent depth dose). These simulations should be done in addition to experimental tests. Not only they are expected to provide us with reference data on the dose absorbed to water (based on the accelerators beam-line models), but they should also help to evaluate accurately the water-equivalence of silica (for photons and protons) and the probe 'invisibility' for their use in IVD.

The PhD student will be strongly involved in all of these tasks (tests and modelling), both at the pre-clinical and clinical levels.

Start: last quarter 2021. **Duration**: 3 years. **Location**: The position will be based in Nice (Faculty of Sciences and Centre Antoine Lacassagne), France.

Qualification: This position offers inter-disciplinary training in materials physics, medical physics, whether on an experiment or theoretical level. Applicants must have a Master 2 degree (or equivalent), preferably in medical or materials physics. Candidates should be familiar with materials (semi-conductor/dielectric) physics, radiations and their interactions with matter, medical physics. Programming skills (Matlab or equivalent) will be an asset.

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FIDELIO

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