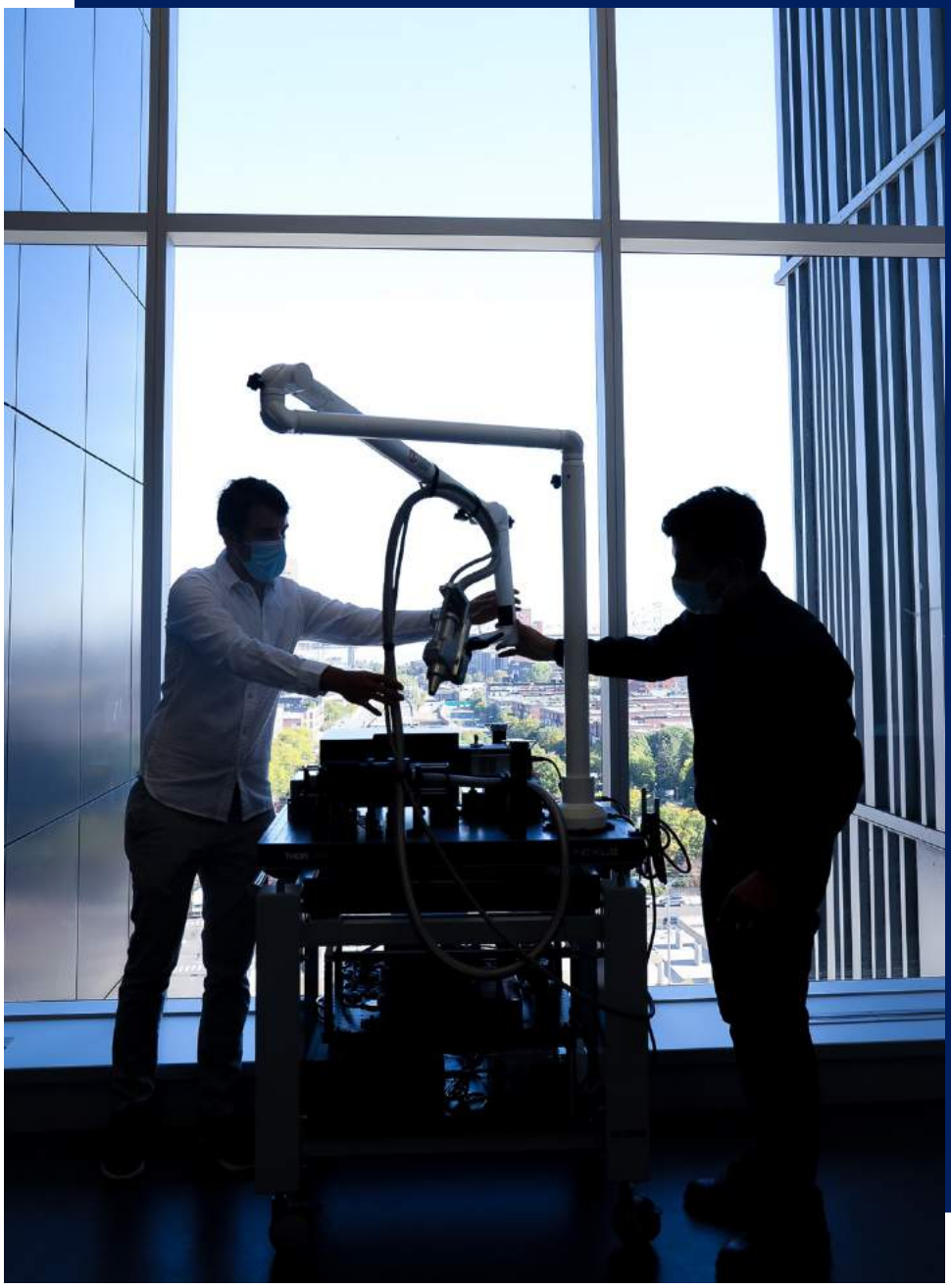

# Optical Medical Probe:
# From the Laboratory to the Operating Room

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**2021**

OPTECH

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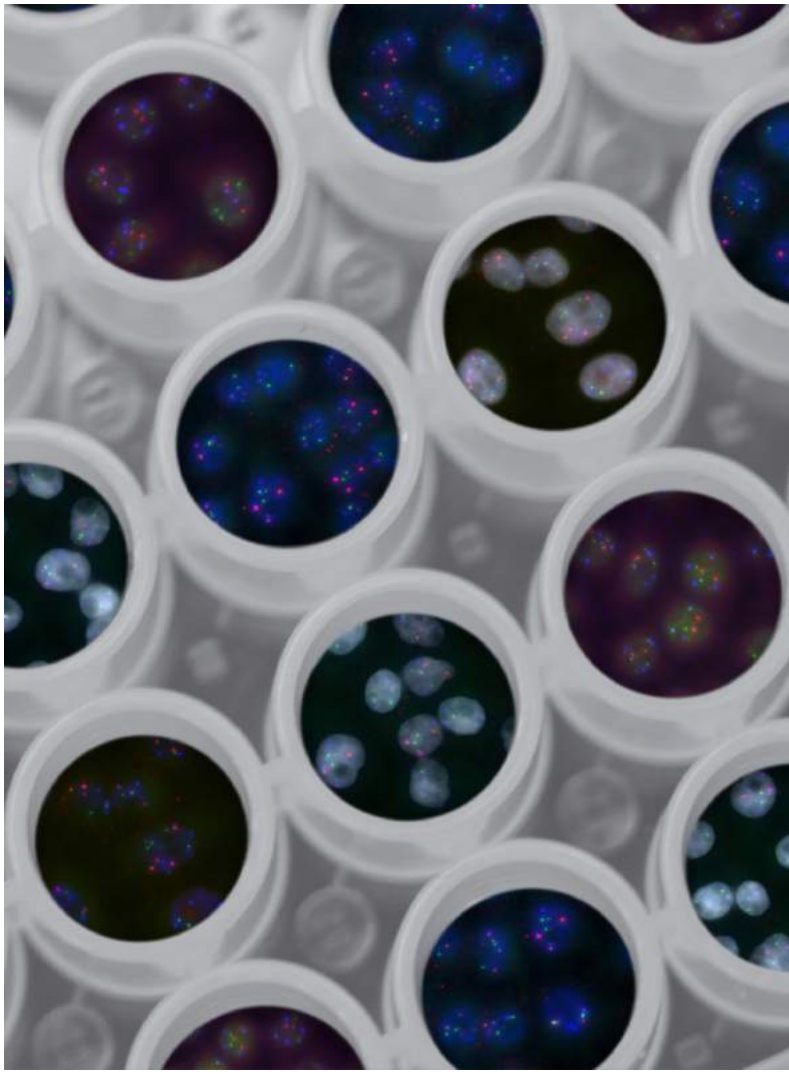
# Objectives

**The objective of this project lies in designing a tool for in vivo characterization of cancerous tissue margins to guide brain surgery (Leblond, 2018).** The surgical tool combines several fields of expertise including optics, optomechanics, Raman spectroscopy, medical imaging and artificial intelligence (AI), the approaches and skill sets of the various international partners that took part in the project.

Belgian research centre Multitel, specializing in the design and manufacture of all-fibre lasers, is working to develop a dual-wavelength, monomodal laser source to eliminate fluorescence effects, a limiting factor in Raman detection (Jean-Bernard Lecourt, 2019).

A study is planned using photonic jets, the specialty of Prof. Sylvain Lecler of the Université de Strasbourg (Sylvain Lecler, 2019), to validate their impact on the injection of the Raman laser excitation signal.



# 01
# Design

# Design

**The first prototypes of this imaging technique were initially developed in the laboratories of Polytechnique Montréal and the Centre de recherche du CHUM (CRCHUM) by Prof. Leblond's team (St-Arnaud K, 2018). The instrument produced a 3.5-mm x 4-mm imagery with a uniform laser projection on the surface to be analyzed.**

The system guides users with a visible-light imagery modality to target the area to be interrogated. A Raman image is then acquired, providing a molecular profile that can be used to differentiate cancerous tissue from healthy tissue. This combination of images allows the surgeon to identify and locate cancerous or pathogenic structures during surgical procedures.

Optech's mandate and contribution to the project consist in designing a new imaging system with the goal of increasing the field of vision (FoV) to 10 mm x 10 mm. This version of the system must also allow for bringing the device under in vivo clinical study to a patient in intraoperative mode.

The main challenge of the increased field of vision lies in the available laser power related to the scan time of the Raman technique. Another feature of the system is the fact that the laser injection is done using a linescan, which increases the power density on the biological tissues, but also different Raman analysis modes.

# Design

The instrument is made up of three distinct sub-systems, each of which has different optical requirements. The optical links between the different sub-systems are provided by fibre optic imaging bundles.

Figure 1 below shows the main components of the system: (a) the probe, (b) the injection arm and (c) the collection arm. (The image is taken from *Daoust, F. et al. 2021*.)

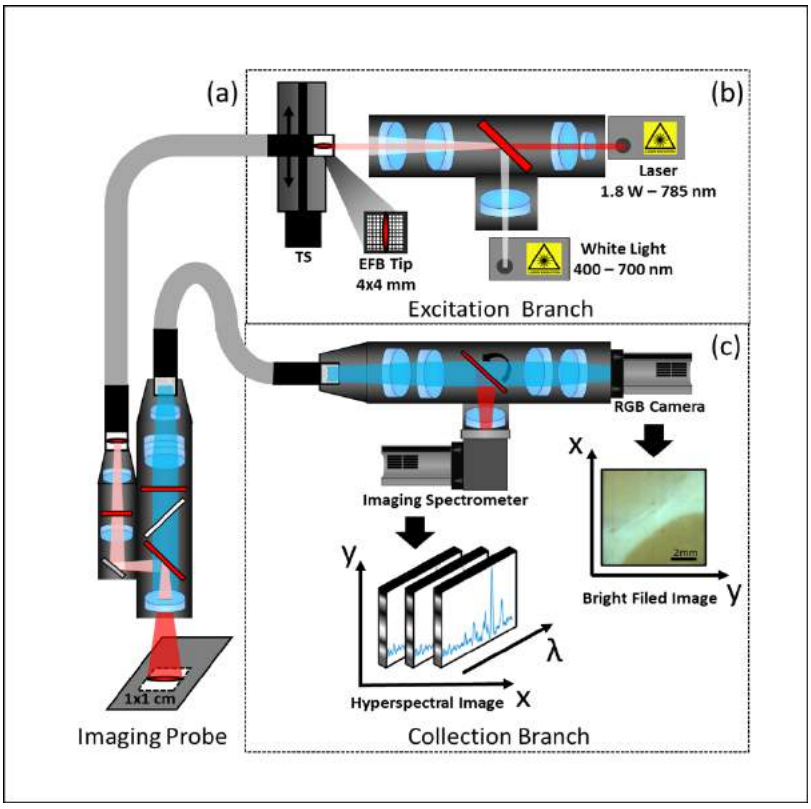



*Figure 1: Diagram of the optical system*

## (a) Imaging Probe

The only component of the system in contact with the patient, it sends the optical illumination signal to the biological tissues in the area of interest and collects the reflected signal using fibre imaging bundles. The strategy of using imaging bundles allows the other sub-systems (electronic, mobile parts, etc.) to be located outside the sterile area.

It must be usable by the surgeon during the operation and be handheld during measurement-taking.

## (b) Injection Arm

The optical elements of this arm are used to combine and inject the system's two sources: infrared light for the Raman component
(785-nm laser) and visible light (410 nm–700 nm) for conventional imaging.

The various optics used here allow for converting the 785-nm laser output (circular fibre optic) to a uniform laser line. This line is scanned onto the imaging bundle by a linear translation motor.

However, the visible lighting must be spatially uniform throughout the fibre bundle so that a uniformly lit image can be collected while using optics common to those of the 785-nm laser.

## (c) Signal Collection Arm

The Raman signal is detected on a spectrometer (spectral range of 800 nm–940 nm) using a CCD 2D sensor chilled to -70 $^{o}$C with one axis supporting spectral data (in $cm^{-1}$) and the other axis corresponding to a spatial dimension (line). To obtain the second spatial dimension of the Raman image, a dichroic mirror, mounted on a galvanometric scanner, scans the physical surface to be analyzed. The dichroic mirror's scan is synchronized with the laser linescan of the injection arm (b) to obtain the Raman hyperspectral image.

This way, each of the pixels making up the Raman image contains the spectral information used to classify the biological tissues.

# 02
# Prototyping

# Prototyping

**The optomechanics were designed and realized after the optics were designed and selected.** The resulting prototype was subjected to various functionality tests to validate the design elements and initial requirements.

CAD tools such as Zemax's OpticsStudio® and SolidWorks® were used for the optical and mechanical designs respectively.

# Probe

**During the optical design and the OpticsStudio® simulations, we designed custom aspheric lenses to compensate for the major chromatic dispersal effects.** These effects are particularly significant due to the extended wavelength band used for visible-light imaging (410 nm–700 nm), but also Raman imaging with excitation at 785 nm (laser) and collection between 800 nm and 940 nm.

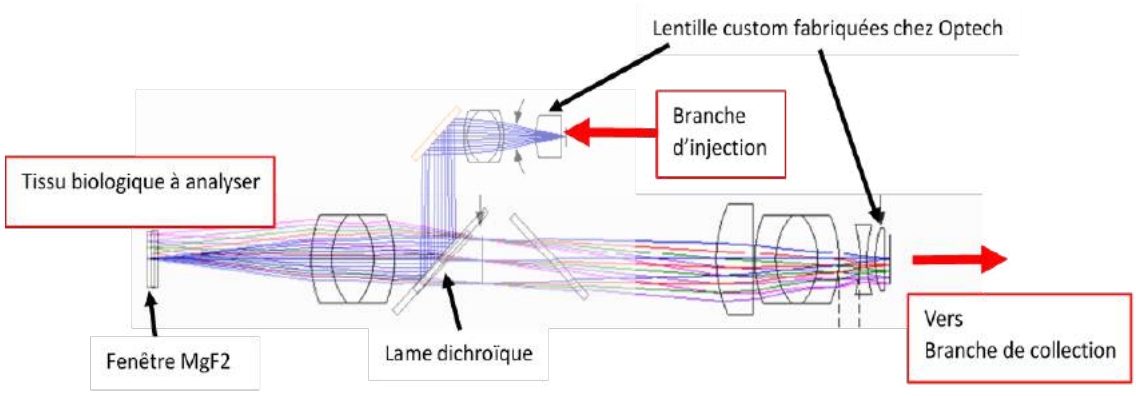



*Figure 2: Design and optical simulation of the probe (OpticStudio ®) using sequential optics (superimposition of the injection and collection lines)*

The custom lenses were manufactured at Optech using our diamond turning lathe, which allows us to manufacture optical components in various materials in-house.

The probe's optomechanics were custom designed for the application. The assembly and precision alignment methods of the internal optical elements were developed to ensure the performances predicted by the calculations.

Since the probe is used in the operating room's sterile area, it must be sterilizable using existing methods: chemical cleaning and/or autoclave. We have also provided for using a tear-off sterile surgical drape (Figure 4) to limit the need for sterilizing the part in contact with the patient, the nose of the probe.

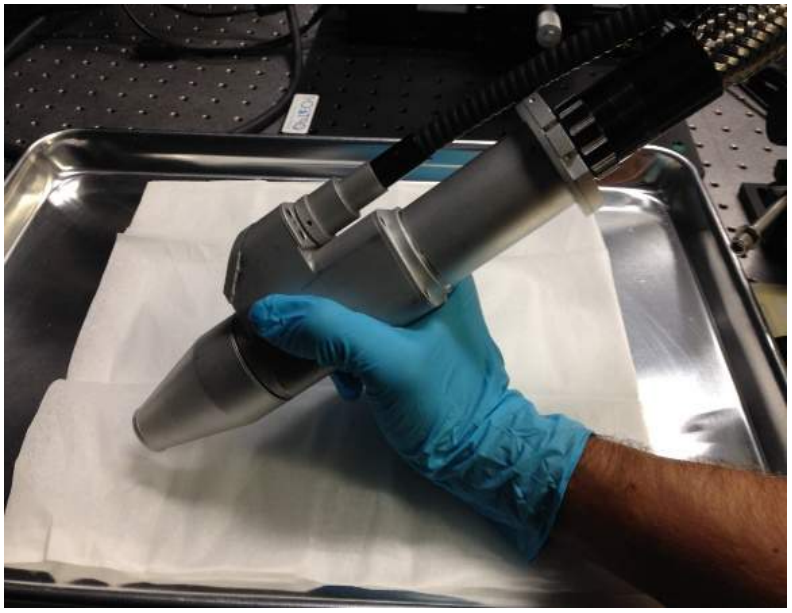


*Figure 3: Assembled Raman imaging probe*

The other systems (injection in Figure 6 and collection in Figure 8) were designed to be integrated into an operating room cart kept at a distance from the sterile area (see Figure 9).

In the following image, we show the optical design of the injection system in the fibre bundle for the 785-nm laser (green beam path) and visible light (blue beam path). The design was realized using the non-sequential module of the OpticsStudio® software for precisely selecting and positioning the lenses.

*Figure 4: Sterile drape wrapping the probe and the imaging bundles*

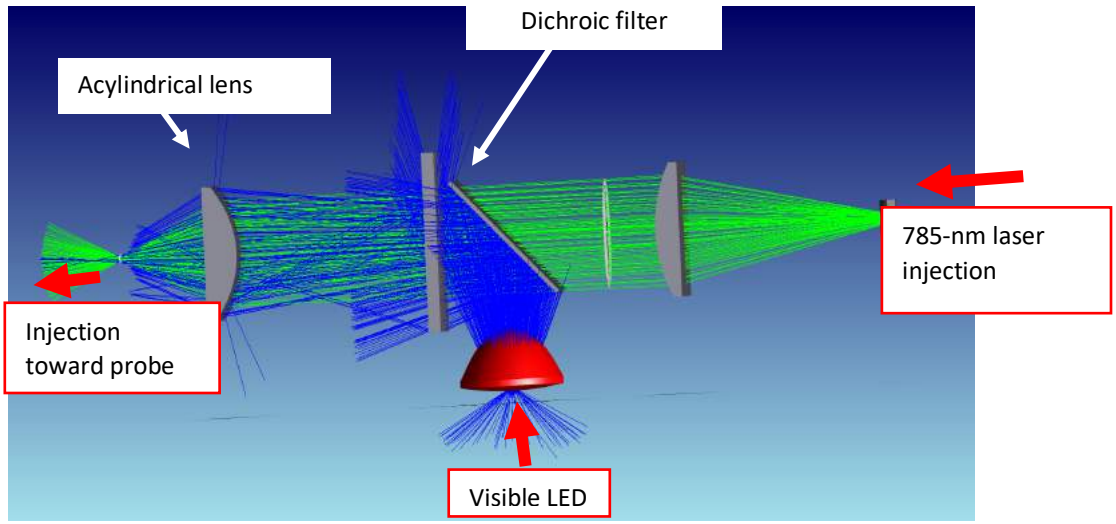



*Figure 5: Design and optical simulation in non-sequential optics (OpticsStudio®)*

The cylindrical lenses were selected and positioned to convert the laser output from a 400 µm–0.22 NA multimodal fibre optic to project a thin, uniform line onto the injection bundle.

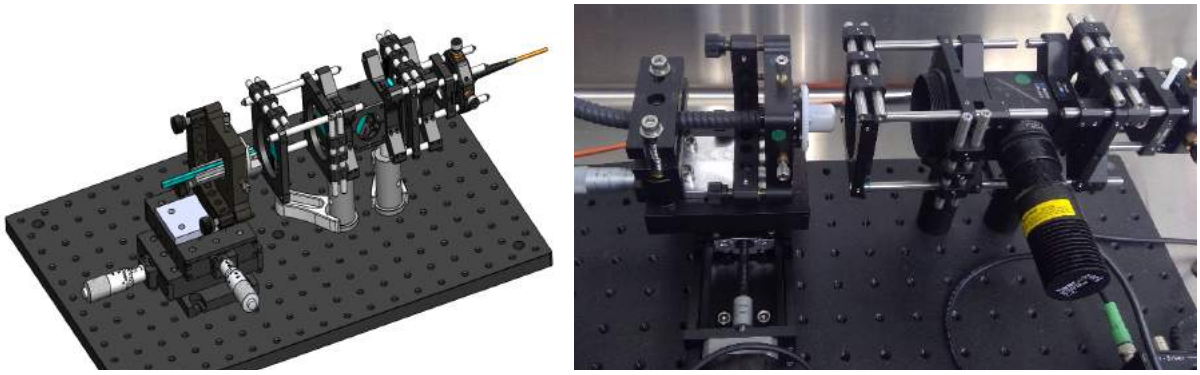


*Figure 6: Optomechanical design and realization of the injection system*

The same optical imaging design phases were carried out for Raman signal collection and visible-light imaging. Optimizing the system could maximize the Raman signal on the spectrometer slot while maintaining image quality.

The difficulty here lies mainly in compensating for chromatic aberrations, given the very wide wavelength band used: 410 nm to 940 nm.

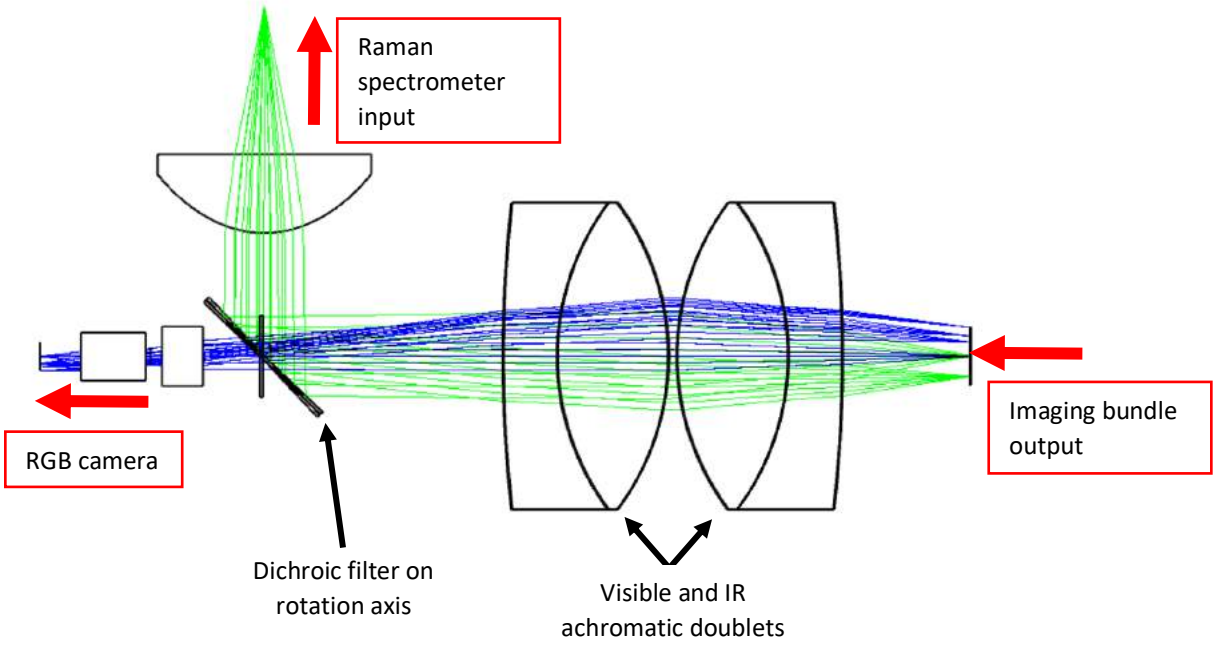



*Figure 7: Design and simulation of optical collection in sequential mode (OpticsStudio®)*

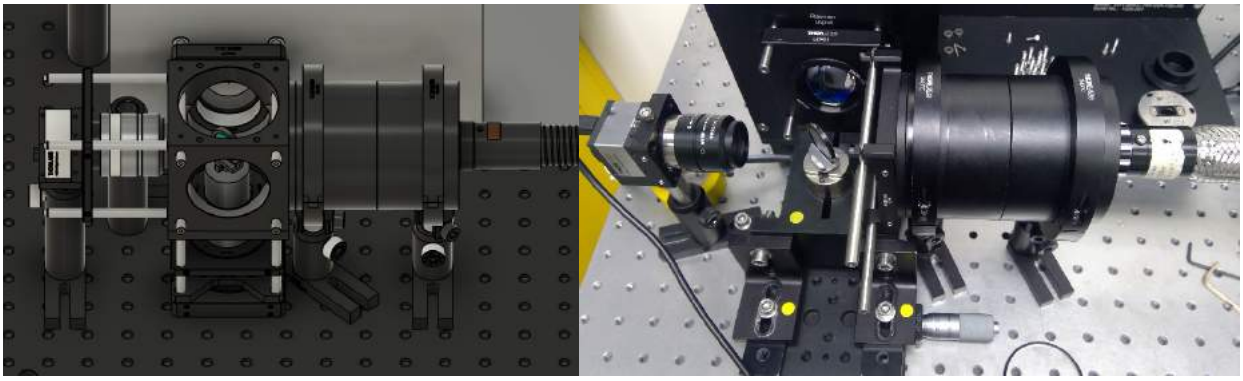


*Figure 8: Optomechanical design and realization of the collection system*

While the system is designed to be handheld, the exposure times are relatively long for the moment (see Table 1 for probe specifications). An articulated arm was added to facilitate handling during surgical procedures.

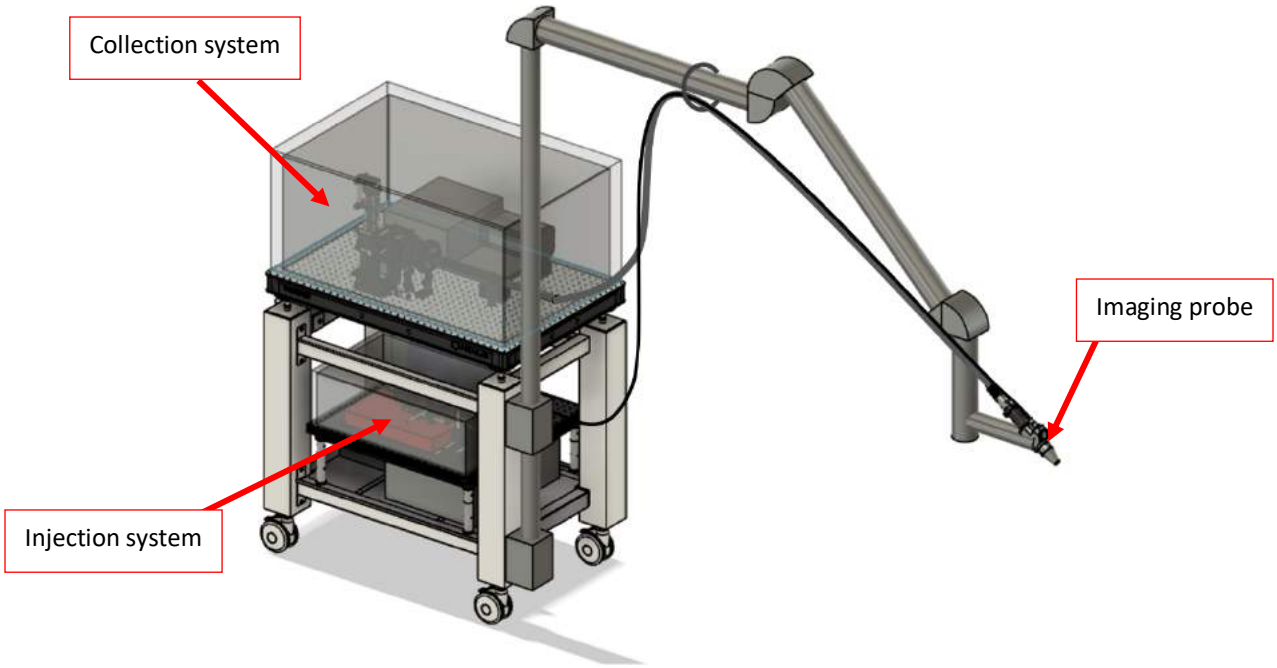



*Figure 9: 3D drawing of the entire system on a cart with probe on an articulated arm*

# 03

# Results and Performances

# Results and Performances

The functionality tests were used to validate the predicted performances during later phases. Several improvement factors were identified to reduce the acquisition time for hyperspectral images and improve the device's performance.

**TABLE 1. Technical specifications of the imaging system**

| | **Specifications** |
|---|---|
| **Field of vision (FoV)** | 95 $mm^2$ |
| **Operating distance** | 40 mm |
| **Number of lines** | 40 lines (9.5 mm x 400 µm each) |
| **Raman spatial resolution** | X axis: 250 µm, Y axis: 250 µm |
| **Raman spectral resolution** | 6 $cm^{-1}$ (to 1085 $cm^{-1}$) |
| **Number of pixels in the Raman image** | X axis: 40, Y axis: 42 |
| **Raman spectral range** | 400 $cm^{-1}$–1,900 $cm^{-1}$ |
| **Acquisition time** | Adjustable: nominal 5 sec/line (total: 200 sec) |
| **Spatial resolution in visible-light imaging** | 50 µm |

# Tests on Biological Samples

The purpose of the optical system consists in classifying organic tissues in order to separate different cell types and determine the margin separating healthy cells from cancerous cells in vivo during surgery.

Classification tests for tissue types were performed first on pork tissues ex vivo. These focused on the distinction between adipose tissues and muscle tissues in order to validate the use of the imaging system.

In Figure 10, with (a) representing a pork chop made up of adipose and muscle tissues, we see the visible-light image (b) as well as a Raman image (c) taken with the probe. The trials on biological tissues were carried out by Prof. Leblond's team at the CRCHUM.

The section of the selected image contains a clear demarcation between the two types of biological tissues (adipose and muscle).

Tissue classification involves training (machine learning) on the spectral data of both tissue types. A model is then established based on the correlation with the main spectrum peaks measured with the Raman probe.

With that correlation, and using machine learning tools, the border between the two cell types can be drawn.

In Figure 12 (b), we can see the superimposition of the visible-light image and the prediction map of the classification model for cell types with the predicted border between the two areas in green.

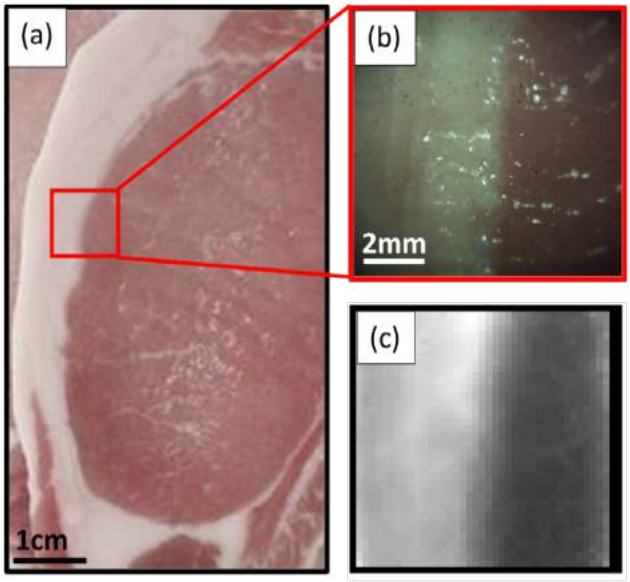



*Figure 10: Tests on biological tissues showing (a) full pork chop, (b) visible-light imaging on a 1cm$^2$ area (FoV) with the probe, (c) image of Raman intensity on the same area (FoV)*

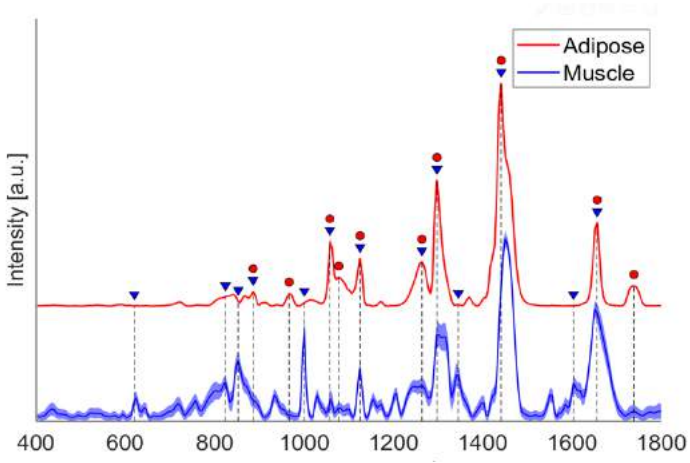



*Figure 11 : Spectres acquis avec l'imageur des tissus adipeux et musculaires pour le porc avec les principaux pics Raman.*

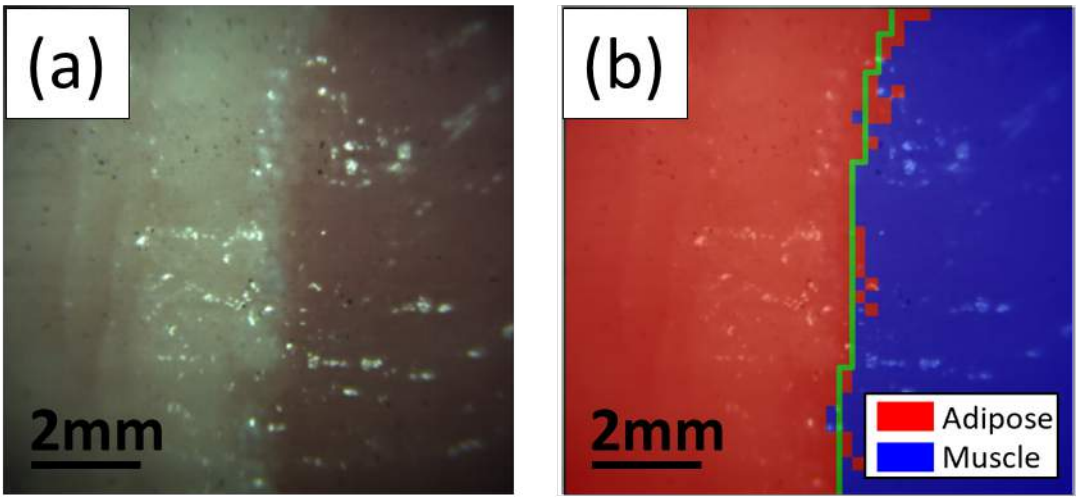



*Figure 12: (a) visible-light image of the exposed area containing an adipose-muscle transition and (b) superimposition of visible-light image and prediction image of the two cell types*

In a surgical context, this visual aid helps the surgeon validate the margins necessary to ensure the cancerous tissues are completely excised and limit the risk of recurrence.

# 04

# Outlook and Future Developments

# Outlook and Future Developments

**Following the trials on biological tissues, several potential improvements were identified, e.g., for improving the ergonomics for handling and quickly installing the probe.** Several optical improvements are also ongoing in connection with adding a new Raman spectrometer recently acquired by the Polytechnique Montréal team.

After clinical studies planned for summer and fall 2021 for breast and brain cancer surgeries, other improvements will also be made, requiring more extensive modifications in terms of lens design, particularly for eliminating fluorescence effects.

Other optomechanical improvements are also planned concerning the probe's handling and ergonomics.

Reliability tests will be necessary, including with the thermal cycling required for sterilization to validate the tool's resistance to environmental effects (temperature, mechanical constraints).

These tests will give us a better grasp of the modifications and improvements required to increase the level of technological maturity with a view to potential medical instrumentation certifications.

# Publications & Acknowledgements

# Publications


1. **Daoust, F. &.-B.-M. (2021).** A handheld macroscopic Raman spectroscopy imaging instrument for machine learning based molecular tissue margins characterization. *Journal of Biomedical Optics (J BIOMED OPT)*.
2. **Daoust, F. O.-M. (2020)**. Large field of view macroscopic Raman line-scanning imaging system for neuro-oncology applications. *SPIE Photonics West - BIOS.* San Francisco.
3. **J. Lecourt, D. K. (2019).** Frequency-Doubled Mode-Lock Fiber Laser Delivering High Energy Picosecond Pulses at 780 nm. *Laser Congress 2019 (ASSL, LAC, LS&C), OSA Technical Digest*.
4. **Daoust, F. &. (2019).** Raman Macroscopic Imaging to Guide Cancer Resection Surgery. *28e Journée annuelle scientifique de l'Institut du cancer de Montréal.* Montréal.
5. **Jean-Bernard Lecourt, F. D.-E. (2019)**. Switchable dual wavelength picosecond fiber laser source operating around 780 nm for advanced Raman spectroscopy . *Proc. SPIE 10908, Frontiers in Ultrafast Optics: Biomedical, Scientific, and Industrial Applications XIX.*
6. **Leblond, F. D. (2018).** Mutli-Modal Wide-Field Optical Spectroscopy Imaging Platform for Biological Tissue Data-Mining,. *International conference on Bio-Sensing and Imaging.* Florence.
7. **St-Arnaud K, A. K. (2018)**. Development and characterization of a handheld hyperspectral Raman imaging probe system for molecular characterization of tissue on mesoscopic scales. *Med Phys*.

# Acknowledgements

**Optech would like to thank the project's international and financial partners for their technical and financial contribution to the project.**

The **Ministère de l'Économie de la Science et de l'Innovation (MESI)** with grant PSR-SIIRI -991

Prof. Frédéric Leblond and his team from the Laboratoire de Radiologie Optique (LRO) at Polytechnique Montréal as well as the Centre de Recherche du CHUM.

Researchers **Jean-Bernard Lecourt** and **Yves Hernandez** from the Multitel research centre as well as the European granting agency Cornet.

Sylvain Lecler, Laboratoire des sciences de l'ingénieur, de l'informatique et de l'imagerie (ICube) at Université de Strasbourg for tests with photonic jets

**Industrial Partners**

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