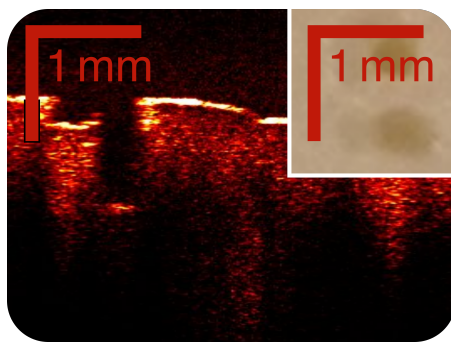


Master Thesis: Cell Damage Spreading in Lesioned and Laser Ablated Cartilage Samples

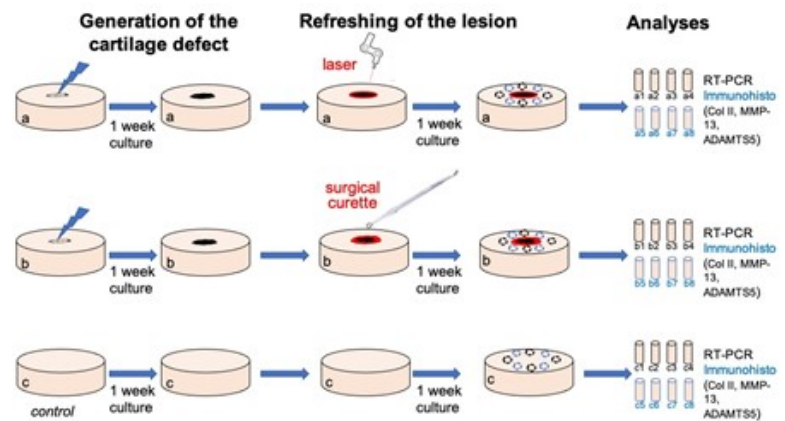
Context: Traumas of knee joints that are quite common in young individuals are the main cause of structural damage to articular cartilage. Such injuries if untreated predispose to degenerative joint pathologies like osteoarthritis [1]. Cartilage defect can be treated by surgically removing the damaged cartilage and filling the generated defect with a precisely shaped engineered cartilage graft [2]. Nowadays, removing the defect cartilage is done manually using surgical curettes. The utilization of laser technology could allow to enhance the integration properties of the therapeutic cartilage graft. Thus, Prof G. Rauter's and Dr. F. Canbaz' groups (DBE) are developing a system leveraging robotic positioning and laser light for precise and controlled tissue ablation (a)[3].

Rationale: Prof A. Barbero's group (DBM) has demonstrated that cartilage tissue surrounding the damaged areas contains cells that expressed degrading enzymes (i.e., MMP-13 and ADAMTS5) at mRNA levels that are higher than those measured in unaffected healthy cartilage and more similar to the ones in osteoarthritic chondrocytes [4]. These results indicate that, a molecular shift toward an "early/pre-OA" phenotype has already occurred in cartilage areas adjacent to the lesion.

Hypothesis: Ablation of cartilage with laser would counteract the tendency of the damage to spread out from the cartilage defect over time.



(a) Example of cartilage ablated with Nd:YAG laser (2 min, 2 Hz, 105.5 mJ).



(b) Experimental design.

Methods (see b):

1. Collection of cartilage samples from human joint specimens.
2. Generation of the cartilage defects.
3. In vitro culture of the samples (to allow for initial cartilage degradation at the margin of the defect).
4. Refreshing of the cartilage defects using the laser or a surgical curette, and additional culture.
5. Analyses on cartilage cylinders isolated from the margins of the refreshed cartilage defects (immunohistochemistry and by RT-PCR to assess cartilage ECM components - type II collagen - and cartilage ECM degrading factors - MMP-13 and ADAMTS5 -).

Benefits:

- Learn to work with human tissue specimens in a sterile way and analytical methods.
- Learn to work with lasers for biological tissue ablation.
- Work in a highly interdisciplinary team of biologists, laser physicists, and robot engineers.

Requirements:

- Solid background in biology.
- Experience with histology and RT-PCR analyse and cell culture would be helpful.

References:

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- [2] M. Mumme et al. "Nasal chondrocyte-based engineered autologous cartilage tissue for repair of articular cartilage defects: an observational first-in-human trial." *The Lancet*, 388(10055), pp. 1985-1994, Oct. 2016. doi.org/10.1016/S0140-6736(16)31658-0
- [3] C. Duverney et al. "Sterile Tissue Ablation Using Laser Light - System Design, Experimental Validation, and Outlook on Clinical Applicability." *J. Med. Devices*, 15(1), pp. 11104/1-11104/12, Mar. 2021. doi.org/10.1115/1.4049396
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