MULTIMODAL MOLECULAR PROFILING TO PREDICT PATIENT OUTCOME AFTER CARTILAGE REPAIR SURGERY

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Prediction model for cartilage repair

Young adults with cartilage defects have a severely increased risk for the development of osteoarthritis later in life if not treated accordingly [1, 2, 3]. Adequate treatment of these defects and better phenotyping of these patients can contribute to the early detection of osteoarthritis and is critical for a delay in osteoarthritis development later in life. Which treatment applies to which patient is currently determined based on the surgeon's experience, as well as MRI, the appearance and size of the defect, and the patient's age and BMI. Nevertheless, some of these patients develop osteoarthritis or require a second surgery in the following years. Combining multiple analysis methods and patient outcome measures, this study aims to build a predictive model, using a multimodal methodology, for patients undergoing cartilage repair surgery. We combined data from fifty-three patients, including patient characteristics, pre and post-operative questionnaires, MRI, as well as a combination of in-tissue mass spectrometry analysis (lipids and proteins) of the infrapatellar fat pad (IPFP) with histology.

Multi-modal methodology

Fifty-three snap-frozen IPFP explants, collected during cartilage defect surgery were cut into two pieces. One was used for lipid analysis using Rapid Evaporative Ionization Mass Spectrometry (REIMS) and one for cryosectioning and proteomics analysis using tandem Liquid Chromatography Mass Spectrometry (LC-MS/MS). Lipid analysis was performed at five different locations per explant with a diathermic knife linked to a REIMS ionization source coupled to a XEVO G2-XS qTOF to collect lipid spectral profiles in negative ion mode. REIMS has already been used as a method for drug detection, tissue identification, and classification. Therefore, this technique could function as possible prognostic or diagnostic tool in cartilage repair surgery. After analysis, the explants were embedded in paraffin for histological analysis.

Cryosections were made of the remaining part of the IPFP for protein analysis. Proteomic analysis in positive ion mode was performed on a Thermo Scientific Ultimate 3000 Rapid Separation UHPLC system, coupled to a Q-Exactive HF mass spectrometer, running in data-dependent acquisition mode.

Lipid and protein data were correlated to patient outcome (questionnaires, including pain scores), patient characteristics (e.g. age and BMI), MRI (hoffitis/synovitis), and histology (Hematoxylin and Eosin, fibrosis and inflammation) (Figure 1).

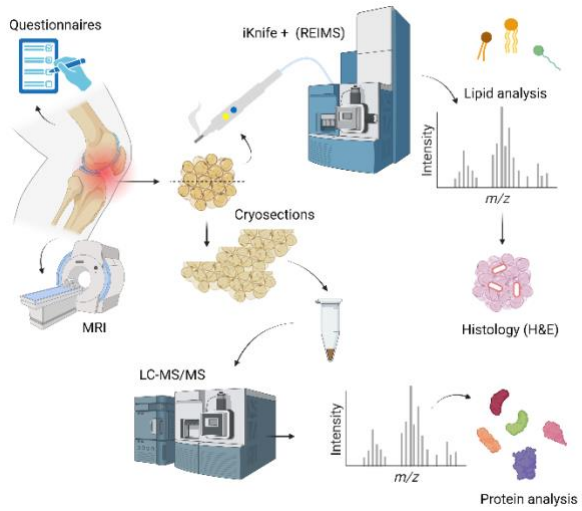

Figure 1. Schematic overview of the multimodal workflow. Created with BioRender.com.

To our knowledge, this is the first study using REIMS (lipids) and LC-MS/MS (proteins), together with additional patient outcome parameters on the IPFP to build a possible prediction model for cartilage repair surgery. Statistical analysis showed the importance of every data outcome parameter of patients after cartilage repair surgery. We were able to build a classification model that can help predict patient outcomes after cartilage repair surgery to help improve surgical decision-making and improve patient outcomes.

References

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