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Amsterdam UMC
Universitair Medische Centra

Bachelorthesis:

Combining needle arthroscopy with near-infrared spectroscopy to assess articular cartilage quality

Faculty: Engineering Technology, University of Twente
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1 Abstract

Osteoarthritis (OA), a common articular cartilage disease, is characterized by limited tissue regeneration due to the aneural and avascular nature of articular cartilage. OA can result from injury or aging and tends to worsen over time as a chronic condition. Detecting early signs is crucial for prevention of OA, but current techniques like MRI and arthroscopy are insufficient. The aim of this project was to formulate and evaluate hardware design requirements for extending needle arthroscopy with NIR spectroscopy for more accurate and quantitative cartilage evaluation.

The design requirements were formulated through literature review and experts interview in the Amsterdam UMC. It was chosen to focus the project on the Arthrex® Nanoscope needle arthroscope. Based on the information achieved from this, a pilot study was done using a spectroscopic method. In this pilot study spectroscopic measurements were conducted on rabbit cartilage. The left and right femur of a rabbit from which the femur head was cut off, were examined. The cartilage sample was divided into 10 measurement points which were measured 4 times each, using two different diameter spectroscopic fibers. One measurement point of the cartilage was deliberately damaged. The data obtained from these measurements was analysed using MATLAB.

Literature review and experts interview reveal that the Nanoscope has limited space for a spectroscopic device, emphasizing the importance of maintaining its diameter. As a result from this, Single fiber Reflectance Spectroscopy (SFRS) is identified as a promising method for spectroscopic measurements through the Nanoscope sheath, because it has a compact design with micron-sized fibers. The results from the pilot study were that using SFRS it is possible to successfully distinguish between damaged and undamaged cartilage. The measurement point with intentionally made damage showed a lower reflectance in comparison with 'healthy' cartilage. Taking into account the results regarding the dimensions of the Nanoscope as well as the functionality of SFRS, hardware design requirements could be formulated.

There are limitations that come with the project's results. In the pilot study, differences in the spectrum are only visible in the visible light wavelength range, not in the NIR range. This restricts the information about cartilage composition. The amount of data obtained from the pilot study was limited, which might be a factor. Therefore, it is necessary to repeat the research to gather more data. Another constraint is the orientation of the fiber tip in SFRS for cartilage quality evaluation. Optimal contact between the fiber tip and cartilage is of great importance, considering the polished angle of the fiber and the curvature of the cartilage sample. The determined optimal polishing angle is 15 degrees. However, achieving a considerable physical angle with the fiber is challenging due to the sideways insertion of the Nanoscope in the joint.

Contents

2 Introduction

2.1 Articular cartilage

Articular cartilage is hyaline cartilage with a glassy-smooth texture that acts as a protective covering for the surfaces of adjacent bones. [1] This shielding tissue covers articulating bones in arthrodial joints. It protects the bones from damage and minimizes mechanical stresses during joint loading. [2] This hyaline cartilage can be subdivided into four separate horizontal layers; the superficial, transitional or middle, deep and calcified zones (Figure 1). [3]

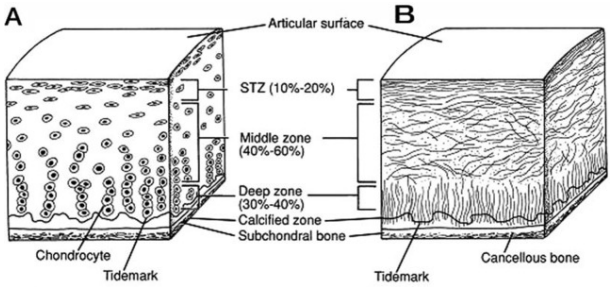

Figure 1: *Different horizontal layers of hyaline cartilage. [4]*

The superficial layer is a thin layer that functions to protect the deeper layers from shear stresses. [4] It contains tightly packed and aligned collagen fibers as well as flattened chondrocytes. [4] The superficial layer contains the highest concentration of water and has a low proteoglycan content. [3] The responsibility of chondrocytes is the homeostasis of the articular cartilage and the replacement of lost macromolecules. [5] The function of proteoglycans is to counteract compression and generate swelling pressure through their water-attracting properties. [5] The superficial layer interfaces with synovial fluid and plays a crucial part in giving cartilage many of its tensile characteristics. These characteristics enable cartilage to withstand the various forces, such as shear, tensile, and compressive forces, that occur during articulation. [4] The transitional or middle layer lies directly underneath the superficial zone. It consists of an increased content of proteoglycans, spherical chondrocytes, and thicker, obliquely organized collagen fibers. [4] The middle zone functions as the first resistance against compressive forces. [4] However, the greatest resistance against compressive forces is given by the deep layer, because of the greatest amount of proteoglycans. [4] This zone contains columnar arranged chondrocytes, parallel to the collagen fibers, which are arranged in large bundles (fibrils) randomly. [4] [3] The deep- and calcified layer are separated by the tidemark. [3] The calcified zone has the vital function of securing the cartilage to the bone. [4]

2.2 Osteoarthritis

Cartilage changes that occur in patients suffering from OA include softening, fraying/splitting, and erosions. [5] These changes are induced by the loss of proteoglycans and its composition. It seems that the breakdown of proteoglycans through proteolytic degradation results in a reduction in the length of the proteoglycan chains and hinders the formation of typical macromolecular complexes. [5] The superficial zone of the articular cartilage is affected first. [5] Normally, cartilage metabolism balances the synthesis and degradation of the matrix components. In OA, the metabolism is disturbed and therefore there is more degradation than synthesis. [6]

It is not yet fully known why this degeneration occurs, but chondrocytes are thought to be impaired by mechanical and enzymatic factors. [7] [2] During the progression of OA, proteoglycan content decreases rapidly. Figure 2 shows the difference between healthy and degraded cartilage. Although collagen content inside the cartilage is not demolished, the arrangement of collagen fiber is heavily disturbed. Collagen disruption reduces the tensile stiffness and strength of the articular cartilage. [5]

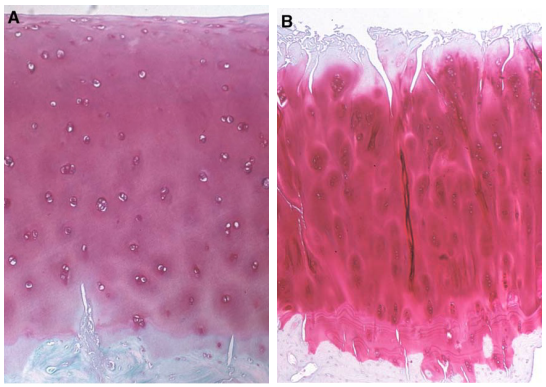

Figure 2: *A) Healthy cartilage B) Degraded cartilage [5]*

2.3 Current cartilage evaluation techniques

Currently, the most important methods for cartilage quality evaluation are MRI and arthroscopy. MRI is a non-invasive method and has a high validity for evaluating cartilage lesions in joints (Figure 3. [9] Despite this, the accuracy of MRI remains low for the detection of initial lesions. [9] A specialized method for assessing early chondral lesions is dGEMRIC (Delayed Gadolinuim-Enhanced MRI of cartilage). This technique does have disadvantages like the fact that intravenous administration of a contrast agent is needed. [10] Arthroscopy is a minimally invasive technique used for the diagnosis and treatment of joint issues. An arthroscope is an optical system that can be inserted in the joint space (Figure 4). The arthroscope is connected to a video camera and light source with which, after insertion in the joint space, the interior of a joint can be observed. [11] Although arthroscopy is a conventional imaging method, it is, like MRI, quite insufficient to diagnose OA in the early stages of the disease. [12] During arthroscopy, the surgeon can use a blunt arthroscopic hook to indent the cartilage. This gives a feel for the softening of the cartilage on top of the visual changes that can be seen via the image from the arthroscope. Several disadvantages of using this technique are that the technique has a low spatial resolution and therefore lesions that lay deeper into the cartilage may go unnoticed. It is also difficult to visibly locate differences in the white mass of the cartilage and obtain all required angles to visualize the whole area of the cartilage. In addition to this, arthroscopy is an invasive method that requires epidural anesthesia. For this reason, arthroscopy must be carried out in surgical conditions. [13]

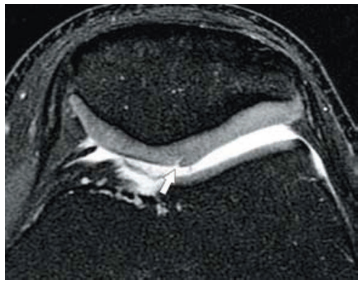

Figure 3: *Axial MRI image showing a chondral lesion on the lateral facet of the patella, indicating grade II chondropathy (arrow). [8]*

Figure 4: *A standard arthroscope manufactured by Arthrex® [14]*

2.4 Needle arthroscopy and near-infrared spectroscopy

Recent advances have been made in the field of evaluation of articular cartilage. Research on a relatively new technique called needle arthroscopy has shown promising results for the assessment of cartilage in an outpatient clinic. [15] Since this arthroscope has smaller dimensions, it can be used with smaller incisions and in areas where tissue must not be disrupted. Needle arthroscopy is promising since it could be a more

efficient and cost-saving alternative to traditional arthroscopy. [16] A needle arthroscope often used for these purposes is the Arthrex® Nanoscope™. [15] [16] To create a more accurate method to assess the extent, level and size of cartilage damage, the use of near-infrared spectroscopy (NIRS) has great potential. NIRS studies molecular vibrations caused by CH, OH and water bonds which can be visualized as broad peaks in a NIR spectrum. [17] Research has shown that it is possible to monitor the progression of OA by NIRS. This can be done by analyzing changes in the spectrum. For example, an increased absorption due to more severe cartilage degradation is mostly caused by increased water content. [18] There already have been several studies on traditional arthroscopy combined with near-infrared spectroscopy to evaluate cartilage quality, showing that NIRS could be an useful addition to the assessment of cartilage quality. [19] [20]

2.5 Problem Analysis

One of the most common diseases in articular cartilage is Osteoarthritis (OA). Osteoarthritis can be the cause of joint pain, restriction of mobility and instability of joints. Since OA is a chronic condition, it will get worse over time. In aging populations, this means that OA causes a high burden on health-care systems. [21] OA can also be caused by several joint injuries, which can affect people of all ages. [12] Because articular cartilage is an aneural and avascular tissue, it has limited self-healing properties. [4] When cartilage in a particular spot is injured, the nearby tissue experiences more pressure and strain. As a result, this extra stress makes the tissue more prone to degeneration and development of OA. [12] For this reason, it is important that preliminary signs of OA can be detected from an early stage on since this can stop the progression of the disease and further development of OA. [12] Since current cartilage quality evaluation techniques like MRI and arthroscopy are lacking in diagnosing the early stages of OA, a more quantitative and reliable technique is needed.

3 Objectives

The objective of this project is to formulate and evaluate requirements to quantitatively assess cartilage quality using NIR-spectroscopy as an extension of needle arthroscopy. The project focuses specifically on hardware requirements for combining needle arthroscopy with NIRS.

3.1 Initial design requirements

At the start of this project, initial design requirements can be formulated. During this project, these requirements will be extended and improved toward hardware requirements. The initial criteria are:

- The product must be able to evaluate cartilage quality through needle arthroscopy
- The product must be able to evaluate cartilage quality through NIR spectroscopy

It is relevant to investigate what studies have already been done with needle arthroscopy, to get a better understanding of the possibilities using this method. To understand what is needed for conducting a spectroscopic measurement, more background information must be provided for the technique of NIR spectroscopy. Furthermore, gaining knowledge about research done involving arthroscopic NIR spectroscopy is essential to understanding how cartilage could be quantitatively assessed within a joint space. For this reason, a literature review involving these topics is conducted in chapter 4. To get insight into the possibilities regarding conducting a spectroscopic measurement within the joint space through the Nanoscope, an optical technician will be interviewed. For extension of the initial design criteria, it is important to acquire knowledge on the procedure using the Nanoscope and what needs to be taken into account regarding the patient. Therefore, an expert with hands-on experience using the Nanoscope is interviewed. Relevant outcomes of these meetings are discussed in chapter 5. In chapter 6 a pilot study is carried out, by conducting spectroscopic measurements on cartilage. The results of the measurements will be evaluated. Using the findings from Chapters 4, 5 and 6, design requirements will be established in chapter 7. Advice for a potential continuation of the extension of the Nanoscope with NIR spectroscopy will be provided in chapter 8.

4 Literature review

As mentioned in Chapter 2 there is a need for a more compact and objectively measurable technique for the assessment of articular cartilage. Both needle arthroscopy and NIR spectroscopy could be potential solutions for this. For this reason, it is desirable to gain knowledge about both techniques through literary review. Furthermore, it is desirable to gain knowledge about what research already has been conducted on quantitative cartilage quality evaluation using arthroscopic NIR spectroscopy. For this literature review, the Pubmed database has been consulted.

4.1 Methods

The literature review has been conducted according to the following method. For acquiring background information about needle arthroscopy, the search query: "needle arthroscopy" was used. There were 113 results in the Pubmed database. Since needle arthroscopy can be used for several different purposes other than cartilage assessment, the search query was refined to: "needle arthroscopy" AND "cartilage". This resulted in 16 results. To investigate how near-infrared spectroscopy could quantitatively evaluate cartilage quality, the search query: "NIRS" AND "cartilage" was used. After screening on available full-text articles this led to 18 results. To do a literary search on what arthroscopic research has already been conducted on cartilage evaluation, the keywords: "cartilage", "arthroscopy" and "NIRS" were added to the search query. This search resulted in 23 corresponding articles. When screening on available full-text articles, 14 remained.

4.2 Needle arthroscopy

Although several needle arthroscopes exist, one of the more well-known needle arthroscopy systems is the Nanoscope™ which is developed by Arthrex® (Figure 5). This arthroscope is called the Nanoscope™ and consists of a 1.9 mm arthroscope, with a sheath of 2.2 or 2.4 mm (depending on the version). This approximately corresponds with a 13G needle, which is normally used for biopsies. [23] [24] The Nanoscope sheath is smaller and more flexible than a traditional arthroscope (4 mm). The arthroscope contains a chip on the camera tip to obtain high-definition imaging and an LED light source. The light source is used for the improvement of visualization of the joint space. [25] The camera system is single-use and has a zero-degree view (meaning it looks straight). The field of view is 120 degrees. [26] Before insertion of the scope, the portal site is determined and injected with a superficial local anesthetic containing lidocaine, epinephrine and marcaine (without epinephrine). The use of a local anesthetic during this procedure enables the use of the Nanoscope in an outpatient clinic and therefore differs from traditional arthroscopy. After the first injection, the joint space is injected with marcaine (without epinephrine). [23] After waiting 5 minutes, the sheath can be inserted in the joint space using a trocar. After insertion, this trocar can be removed and the Nanoscope™ image sensor can be inserted through the sheath. [23]

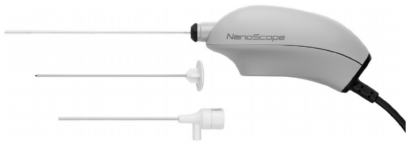

Figure 5: *The Arthrex Nanoscope [22]*

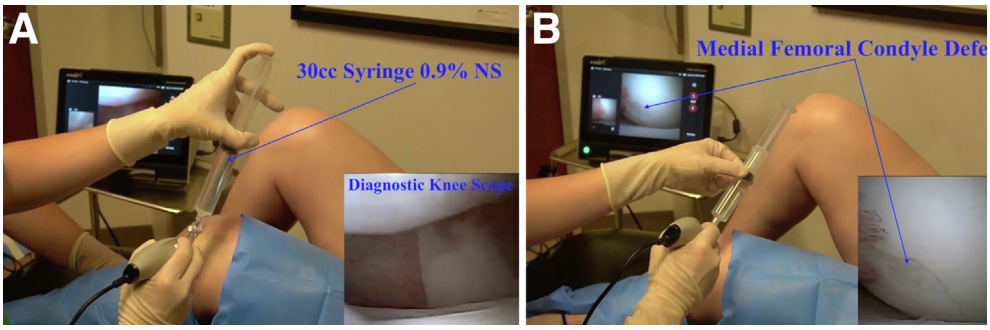

Figure 6: *(A) Shows the view of the lateral side of the left knee. In the inset, an arthroscopic view of the knee through the anterolateral portal can be seen. The joint is insufflated with 30cc of sterile 0.9% normal saline after which extra sterile saline can be added through the one-way stop valve. (B) Shows the view of the lateral side of the left knee. In the inset, an arthroscopic perspective of the left knee is observed through the anterolateral portal site. An osteochondral defect can be seen on the medial femoral condyle. [23]*

A one-way stop valve can be added to the sheath through which saline fluid can flow and insufflate the joint (Figure 6). [16] Using the Nanoscope it is possible to detect defects in the articular cartilage (Figure 6-b). [23] One of the disadvantages of this method is that diagnostic accuracy can be decreased due to a lack of continuous fluid flow during the procedure. [23] The purpose of fluid flow during arthroscopy is to create pressure to minimize bleeding of capillaries and therefore increase visual clarity. [27] Another limitation of needle arthroscopy is that the camera used in needle arthroscopy is smaller and more flexible than in standard arthroscopy, which makes it more fragile. [16]

4.3 Spectroscopic measurement of cartilage

4.3.1 Spectroscopy

The main principle of spectroscopy is the interaction of matter with electromagnetic radiation. [28] This technique is used to gain insights into the structure, composition and characteristics of a substance. Gaining these insights is done by examining the ability of a substance to absorb, emit or scatter electromagnetic radiation. [29] When a molecule is irradiated by certain electromagnetic radiation, it undergoes a transition between states of energy. [29] A molecule can undergo either rotational, vibrational or electronic transitions, which can be triggered by the absorption/emission of microwave, infrared or UV/visible radiation, respectively. [28]

4.3.2 Reflectance spectroscopy

The concept of reflectance spectroscopy is analyzing light that is reflected from tissue over a certain wavelength range. The amount of reflectance of a tissue is influenced by its scattering and absorption properties (Figure 7). Absorption means that the energy of a photon is absorbed and converted into heat energy. [30] In the infrared (IR) region of the spectrum, tissue can absorb photons through vibrational transitions. Molecules in the tissue can vibrate at specific frequencies, and when the energy of the incident photons matches these vibrational frequencies, the photons are absorbed, causing the molecules to vibrate more vigorously (Figure 8). [31] The scattering of photons occurs because of a mismatch in refractive index at particle-air and particle-particle gaps, which is part of the anatomical features of tissue. [32] [33] In cartilage, the greatest part of light is scattered and only a small part is absorbed. [34] There are different types of scattering processes that can be induced by NIRS. Photons are scattered elastically during a process called Rayleigh scattering, meaning that the photons do not change energy and wavelength concerning the incident photons. Because Rayleigh scattering does not contain chemical information, it is commonly considered a background signal in NIRS.

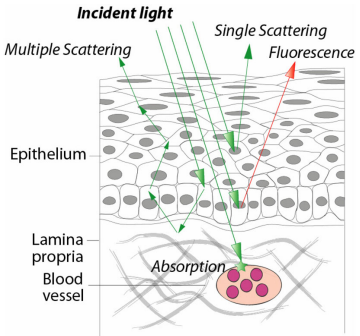

Figure 7: *Schematic representation of the absorption and scattering of photons by the skin. [30]*

Rayleigh scattering occurs when the sample particles have a diameter that is 1/10 of the wavelength of the incident photon. [29] Another scattering process that can occur is Raman scattering, which is inelastic. During Raman scattering, the scattered photons either have a shorter or longer wavelength (energy) than the incident photon, because of interactions with molecular vibrations. Through Raman scattering, information about the molecular structure and composition of a sample can be obtained. [29] Factors that contribute to the extent of scattering of a sample are sample density and porosity. [33] To be able to understand optical behaviours in tissues, separation of absorption and scattering events of a sample are needed. This enables the correlation of chemical and physical features with absorption and scattering properties. Through separation, the absorption and scattering spectra can be obtained which can be used for quantitative and qualitative applications. [33] The light propagation through a sample can be described through the radiative transfer theory (radiative transport equation, RTE). A commonly used method for the radiative transfer theory is the Monte Carlo (MC) simulation. [33] MC simulation is a statistical technique that samples the probability distribution for various photon migration parameters, including step size, scattering direction, internal reflection, and boundary interactions. These parameters are generated using random number generators. [33] By employing these functions, the movement of individual photons is tracked in a step-by-step manner as they move through the medium. [33] Consequently, the distribution of light, including reflectance and/or transmittance, is recorded based on these individual photon paths. As the number of photons simulated in the process increases significantly, the Monte Carlo simulation converges towards an analytical solution to the Radiative Transfer Equation (RTE) for describing the distribution of light. [33]

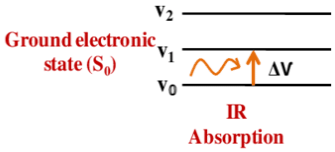

Figure 8: *Schematic representation of IR absorption through a vibrational transition. [35]*

4.3.3 Near-infrared Spectroscopy

To be able to quantitatively evaluate the cartilage quality, a relationship must be modelled between NIR spectral data and reference parameters. This can be done using artificial neural network (ANN) which is a computational model based on the structure and functioning of biological neural networks. [19] Artificial neural networks are good at understanding complicated, not-so-straightforward relationships in data, which makes them quite useful in the world of machine learning and artificial intelligence. [36] For this reason, ANNs can correlate certain features of the NIRS spectrum with the desired measurements of cartilage quality. [19] The main components of cartilage are: water, proteoglycans and collagen. The most prevalent bonds found in these tissue components include OH, SH, NH, CH, and PO4 bonds. NIR spectroscopy is sensitive to CH, NH, OH and SH bonds. Water, making up the majority (up to 80%) of cartilage composition, significantly affects the spectral response of cartilage due to the presence of the OH bond (Figure 9). [19] In the case of cartilage degradation concentrations of water and collagen change and therefore the spectrum also changes. It was discovered by Spahn et al. that these composition changes correlate with changes in the NIR absorption spectrum and therefore can be detected using NIRS. [20] [37] The near-infrared (NIR) spectrum consists of wavelengths from 700 – 2500 nm. If the energy of the NIR radiation matches the frequency of a certain bond within a molecule, the radiation is absorbed. By determining the wavenumbers of the energy absorbed, it can be

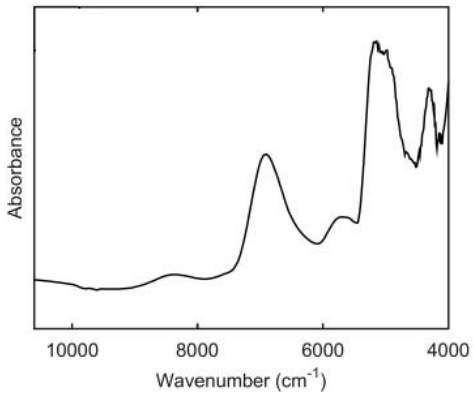

Figure 9: *NIR absorbance spectrum of articular cartilage. Bonds that can be seen in this spectrum are C-H (2nd overtone) (8820 - 8060) & (8695 - 8197cm^{-}1), O-H (7460 - 6780cm^{-}1) & (7280 - 6040cm^{-}1), Free water (6890cm^{-}1), C-H (first overtone) (5720 - 5500cm^{-}1), Bound and free water (5200 cm^{-}1) [35]*

defined which bonds a certain compound contains. [38] NIRS has a penetration depth of about 1-10mm and is therefore suitable for investigation of the composition of cartilage. [37]

4.4 Arthroscopic NIRS

The oldest article about arthroscopic NIRS was published in May 2007 and is a pilot study in which NIRS is tested (in vivo) as a new method for cartilage evaluation. [9] Evaluation of low-grade cartilage lesions by NIRS was compared to arthroscopic findings and radiography and MRI evaluation. The conclusion was that NIRS could indeed be used for the quantitative distinguishment of healthy and low grade cartilage lesions by determining the relationships between the parameters using the Pearson correlation coefficients. [9] This was also concluded by Hofmann GO. [37]. Arthroscopic NIR spectroscopy is often conducted using a custom curved fiber optic probe. [19] [12] The fiber optic probe is designed to measure perpendicular to the cartilage, which is a challenge itself because of limited access in the narrow joint space (Figure 10). [13] Even though arthroscopic NIR spectroscopy is showing great potential to improve cartilage evaluation, one of the disadvantages is that this method is still quite invasive, since the diameter of the probe is around the same as most traditional arthroscopes, approximately 4 mm. In addition to that the procedure must be carried out in a surgical setting, which is time-consuming and expensive. [19]

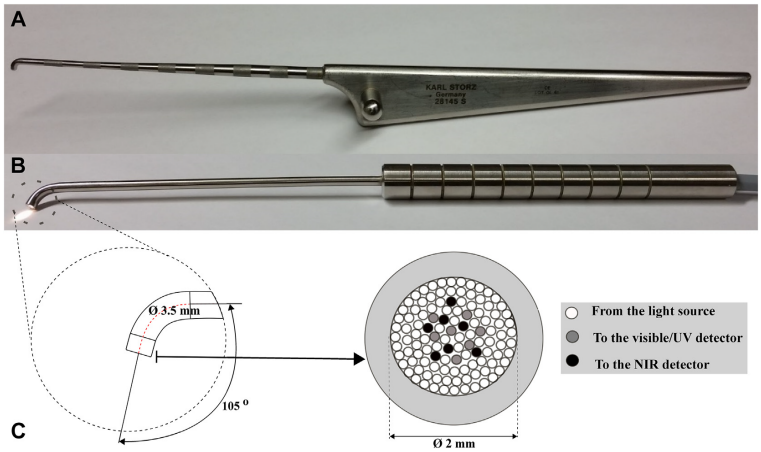

Figure 10: *(A) A traditional arthroscope hook. (B) Custom curved fiber optic probe. (C) Schematic representation of the tip of the curved fiber optic probe containing optical fibers for emitting and collecting light. [13]*

5 Interview experts

Using the background information gained from the literature review in chapter 4, interviews were held with experts on how to incorporate NIRS into the Nanoscope. Alex Walinga is a PhD candidate at the Orthopedic Surgery department of the Academical Medical Center in Amsterdam and has hands-on experience with the Nanoscope. He has been interviewed on the use of the Nanoscope. It has been discussed what needs to be taken into account when inserting the device in the joint space. For example it is important to investigate the movement space of the Nanoscope within the joint, since this can limit conducting a spectroscopic measurement. Furthermore, information on possible adjustments that could be made to the Nanoscope was acquired. To be able to conduct a spectroscopic measurement within a joint space a very compact spectroscopic technique is needed. Knowledge on the possibilities for a compact spectroscopic instrument was gained from Paul Bloemen, who is an optical and technical engineer at the Academic Medical Center in Amsterdam. In the following sections, two compact methods for conducting spectroscopic measurements are discussed. With Paul, it has also been discussed what criteria must be met to conduct a reliable and accurate spectroscopic measurement. The outcomes of the interviews held with Alex and Paul are discussed in the sections below.

5.1 Nanoscope

5.1.1 Movement space

One of the challenges of the use of the Nanoscope is the limited movement ability within the joint space. This is partly because the Nanoscope contains a rigid imaging sensor and partly because there is very limited space within the joint. To successfully conduct a spectroscopic measurement it is desirable to have a 90 degrees angle between the spectroscopic instrument and the cartilage. This is a challenge since the Nanoscope is inserted sideways into the joint space and therefore directed parallel along the articular cartilage (Figure 11). It must also be taken into account that patients qualifying for cartilage assessment already have swelling and complaints about pain. This makes it less pleasant for the patient to be moving around the device a lot to obtain a certain angle.

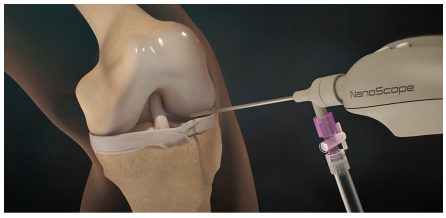

Figure 11: *Nanoscope inserted in knee joint. [39]*

5.1.2 Dimensions

With the camera system having a diameter of 1.9 mm and the sheath of 2.4 mm diameter, there is about 0.5 mm of space left (Figure 12). Depending on what method is used for conducting the spectroscopic measurement, this might be enough space, but it must be taken into account that during the procedure fluid flow must be provided for optimal visualization. The Nanoscope has already been used at an outpatient clinic meaning that local anesthesia can be used. If a Nanoscope with integrated spectroscopic fiber having a greater diameter were to be used, it is unknown whether local anesthesia could still be used. Several solutions for this were discussed during the interview. One of the possible solutions for this challenge could be creating a second portal in the joint. This way there would be a separate portal for inserting the spectroscopic fiber(s) and this would be easier dimension-wise. However, this solution does raise ethical concerns since creating a second portal makes the procedure more invasive. It is therefore desirable that the created prototype does not have a diameter larger than 2.4 mm.

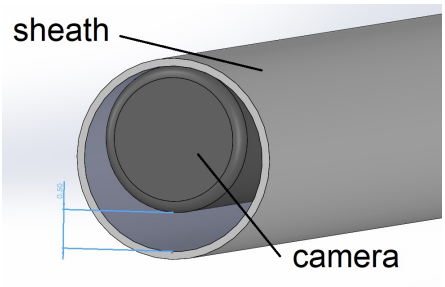

Figure 12: *Illustration of the 0.5 mm space left between the imaging sensor and sheath of the Nanoscope (indicated in blue).*

5.2 Methods for NIRS

5.2.1 Single fiber reflectance spectroscopy

A compact and promising method for conducting spectroscopic measurements within the joint space is single fiber reflectance (SFR) spectroscopy (Figure 13). In SFRS, light is emitted and collected through the same fiber. SFR spectroscopy allows for measurements to be conducted through endoscopes and biopsy needles because SFR fibers typically have a diameter of a few hundred microns. [32]

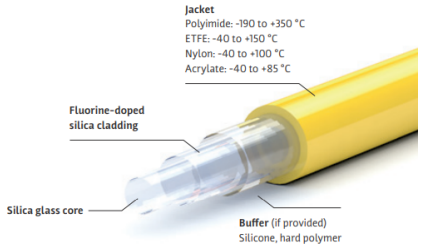

Figure 13: *Close up of the fiber tip of a SFR fiber [40]*

5.2.2 Diffuse Reflectance Spectroscopy

Diffuse reflectance spectroscopy (DRS) is another commonly used technique in the field of medical science for the diagnosis of cancers and various other diseases. [41] In DRS, one fiber is used to emit light while reflecting light is collected through one or more fibers that are at a distance from the source fiber. [32] DRS probes are less compact than SFR fibers since the typical diameter is a few centimeters.

5.2.3 Comparing DRS and SFRS

Since the distance (width) between the source fiber and detection fiber in SFR spectroscopy is 0, the distance the photons travel is generally less than the mean free path. Therefore, the reflection measured by the detection fiber contains photons that underwent many scattering events (diffuse photons) and photons that underwent a few scattering events (semiballistic photons). In DRS the photons generally travel more than the mean free path and therefore the reflected photons have undergone many scattering events. DRS, as the name suggests, thus measures many diffuse photons. Because diffuse photons have undergone many scattering events, they provide valuable information about the optical properties and composition of tissue. [32] Because SFRS is generally less affected by surface properties, it can provide more consistent results. [32].

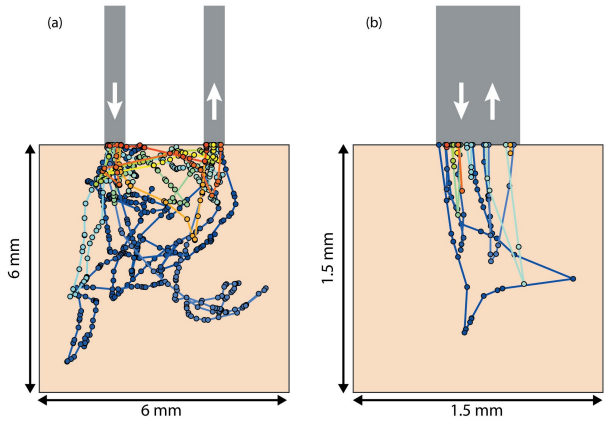

Figure 14: *Schematic of the simulated paths of detected photons for Diffuse Reflectance Spectroscopy (DRS) and Single Fiber Reflectance Spectroscopy (SFRS). Note the differences in scale. The fibers are represented in grey. DRS makes use of multiple fibers for emitting and collecting light (Figure A) and SRFS uses one fiber (Figure B). [32]*

The distance (width) between the source fiber (emitting light) and detection fiber (collecting reflected light) is proportional to the penetration depth of the fiber. Since SFR spectroscopy uses a single fiber for emitting and detecting light, the penetration depth is quite shallow, a couple of hundred micrometers. [42] In addition, in comparison with DRS, the sampling volume of SFR spectroscopy is much smaller. The recorded spectrum is obtained by averaging across the sampled volume, meaning that a smaller sampling volume allows for the detection of smaller changes. [32] The fact that the sampling volume is smaller in SFR spectroscopy than DRS, is visualized in Figure 14.

5.2.4 Back reflection

Since SFRS is a promising compact spectroscopic method, this technique will be investigated further. To measure the reflected light as accurately as possible, certain measures need to be taken. To prevent that a part of the emitted light reflects from the inside of the fiber and travels back up the fiber (back reflection), the tip of the fiber can be polished at an angle. This angle ensures that from inside reflected light does not stay in the fiber core but leaks towards the cladding (outside layer) of the fiber (Figure 15). Therefore the majority of reflected light that will be detected, is reflected by the cartilage. The polishing angle is determined based on the numerical aperture (NA) of the fiber. The NA of an optical system is a measure of its ability to gather and focus light. A higher NA implies that the fiber can collect light over a wider range of angles. The NA is dependent on the core and cladding (outside layer) of the optical fiber. [44] Furthermore, the amount of back reflection is dependent on the reflection coefficient of the medium.

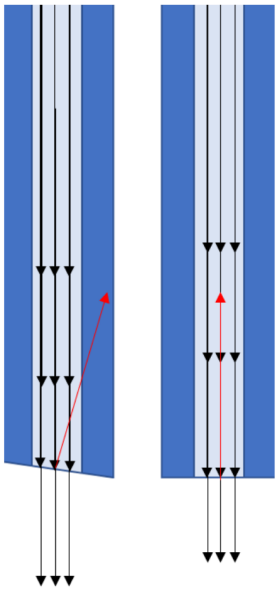

Figure 15: *Fiber polished at an angle to prevent emitted light from directly reflecting back into the fiber core, as is illustrated by the red arrow in the most right Figure. Instead when using a polished fiber tip, the from inside reflected light leaks towards the cladding (outside layer) of the fiber and is not detected. This is illustrated in the left Figure by the red arrow. [43]*

5.2.5 Criteria for reliable measurements using SFRS

Calibration of the optical fiber must be done to obtain reliable measurements. A dark spectrum must be measured by switching off all light sources (surrounding light included), to determine the background noise that is detected by the spectrometer. The reference spectrum can be measured by using a 'perfectly' reflecting surface like either a mirror, spectralon (white solid) or intralipid (white liquid). [45] Which substance to use is dependent on the spectrum in which is measured. Using this reference and dark spectrum, the amount of light reflected by the measured sample is relative to the reflectance of the reference substance and the background noise.
Optimal measurement of reflected light is achieved when the surface of the tip of the fiber is held perpendicular to the tissue and most of the reflected light is collected. Although these SFR fibers have a very small diameter, they do have limitations concerning the curvature of the fiber. The bending radius of an SFR fiber must be at least 5 times the diameter of the core. Preferably a measurement using SFR spectroscopy is conducted using two fibers with different diameters. This is called multi-diameter SFR (MDSFR). MDSFR is preferred since it can be used for tissue characterization and depth profiling since different diameters have different penetration depths. MDSFR enables mathematical modelling and inverse analysis based on Monte Carlo simulations, with which the absorption and scattering coefficients of a medium can be determined. [46]

6 Testing cartilage quality evaluation using SFRS

6.1 Introduction

As stated in chapter 5, SFRS is a promising technique for conducting spectroscopic measurements in a small space. To gain knowledge about the use of SFR spectroscopy for the evaluation of cartilage quality, a pilot study was conducted. In this study, it is investigated whether it is feasible to conduct spectroscopic measurements while handholding a SFR fiber. In the following sections, the experimental phase will be described.

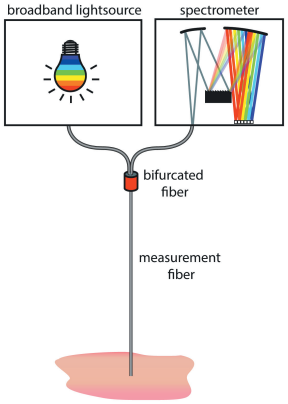

Figure 16: *Experimental setup for measurements using SRFS. [32]*

6.2 Materials and Methods

6.2.1 Experimental setup

The experimental setup is sketched in Figure 16 and consists of a broadband light source and spectrometer which are both connected to a bifurcated fiber. This bifurcated fiber consists of 2 fibers, one emitting and one collecting light. Both of these fibers have a diameter of 100 mu. As can be seen in Figure 16, the bifurcated fiber fuses from two to one wire and is then connected to the measurement SFR fiber through a connection piece. The light source used in this experiment is the Avantus® Avalight-HAL. This is a broadband light source which ranges from 360 - 2500 nm. For this experiment, the Avantus® AvaSpec-HS2048XL-EVO is used. This spectrometer uses the visible NIR-infrared wavelengths and ranges from 400-1100 nm. The bifurcated fiber was self-constructed for the research of Anouk Post. [32] The two SFR fibers used in this experiment are the low OH (meaning they are suitable for wavelengths ranging from visible to infrared) fibers from Ceramoptec®. The fibers have a core diameter of 300 and 600mu (and therefore differ in penetration depth) and a NA of 0.22. The fibers are polished under a 15-degree angle. The 300 mu fiber would be sufficient to fit through the Nanoscope (Figure 12).

6.2.2 Calibration

To obtain a reflectance spectrum, calibration of the fiber must be done. The calibration of the spectrometer was done by saving a dark spectrum and a reference spectrum. Substances used for the calibration were Milli Q and intralipid (Figure 17). The dark spectrum is needed to determine background noise and was acquired by switching off the light source as well as all other lights in the room. The fiber tip was then put in a centrifuge tube containing Milli-Q which is ultrapure water and has very little reflectance. A reference spectrum can be obtained using a substance that has broadband flat reflection, meaning that it has a uniform and consistent reflectivity over a broad range of wavelengths. Such a substance is intralipid, which is a very white substance. This measured reflectance spectrum functions as a reference to all other obtained reflectance spectra. In between recording the dark- and reference spectrum the fiber tip must be cleaned well since any left substance can negatively influence the calibration. The reference spectrum was acquired by switching on all light sources again and putting the fiber tip in the centrifuge tube containing intralipid.

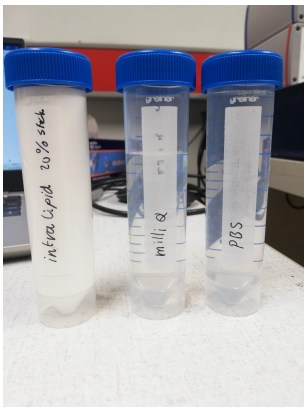

Figure 17: *Substances used for calibration, left: intralipid, middle: milli Q. The right substance (PBS) was used for sample preparation.*

6.2.3 Cartilage samples

For this experiment, the left and right femur of a rabbit were used (Figure 18). In preparation for this experiment, the femur head from both sides was cut off and both pieces were wrapped in gauzes drained in PBS, after which it was frozen. During the experiment, the defrosted samples were placed in 2 Petri dishes and moisturized using a PBS solution. Moisturizing the sample is needed to maintain sample quality.

6.2.4 Conducting measurements

The spectroscopic measurements were conducted according to the following protocol. The sample was subdivided into 10 different measuring points (Figure 18). These measuring points were selected according to visible damages in the cartilage and colour differences. Measurement points 1 and 2 were not examined, because these points were located on two edges of the cartilage and it was not possible to conduct measurements on these edges. Measurement points 9 and 10 were only measured by the 600 mu fiber. The damage at measurement point 8 were made before the measurement by the use of a hammer. Each point was measured 4 times by placing the fiber tip in direct contact with the cartilage, hand-holding the fiber. This was done with the 300mu as well as the 600mu fiber. Prior to the measurement, the orientation of the polished fiber tip was determined by switching off the lights and looking at the orientation of the light emitted by the fiber. Keeping in mind this orientation, the fiber was placed under an angle of approximately 75 degrees, depending on the curvature of the cartilage sample. This was done to obtain optimal contact between the surface of the fiber tip and the cartilage.

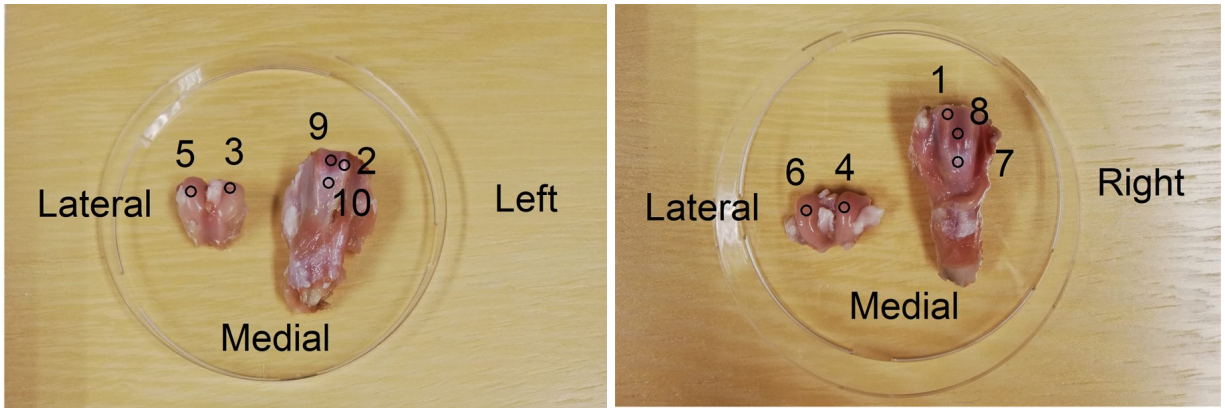

Figure 18: *Rabbit femur cartilage samples which were used for the experiment. For both femurs, the femur head was cut off and can be seen on the left of each petri dish. The samples are subdivided into several numbered measurement points.*

6.3 Data Analysis

To conduct the spectroscopic measurements, the Avantus® Avasoft 8 software is used. Using this software it is possible to continuously monitor the spectrum during placement of the fiber onto the tissue. The spectrum can be paused and then saved as a .RFL8 file. Afterwards, these files can be exported as .xlsx files for further processing using the MATLAB software. Using the MATLAB software spectra can be plotted and compared. The Matlab script used for further analysis of the data can be found in Appendix A.2.

6.4 Results

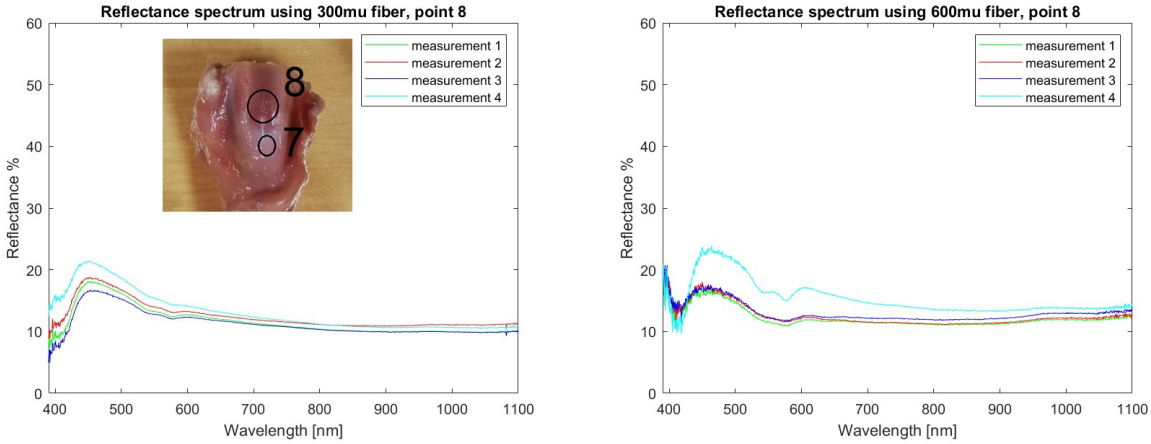

Figure 19: *Reflectance spectra obtained from SFRS measurements using a 300 mu fiber (left) and a 600 mu fiber (right) at measurement point 8.*

The results obtained from the SFRS measurements conducted using the 300 mu fiber and the 600 mu fiber at measurement point 8 can be seen in Figure 19. A complete overview of the results can be found in Appendix A.1. Differences in the measurements are visible quite clearly. Especially in the reflectance spectrum obtained from measurements with the 600 mu fiber, measurement 4 differs a lot from the other measurements. It can be seen that the 300 mu as well as the 600 mu fiber show absorption peaks at 541 and 577 nm are visible clearly (vertical lines in Figure 20).

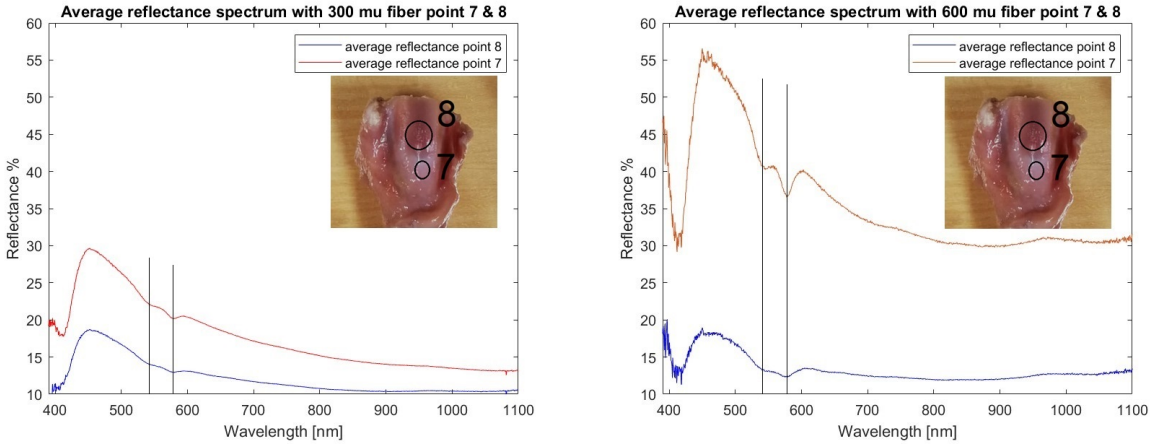

Figure 20: *The average reflectance spectrum for measurement point 7 & 8 using a 300 and 600 mu fiber. Vertical lines indicate absorption peaks at 541 and 577 nm.*

In Figure 20 the average reflectance spectra can be seen for measurement points 7 and 8 using a 300 and 600 mu fiber. These results specifically have been chosen, because there was a known damage difference in the cartilage between points 7 and 8. For both fibers, measurement point 7 showed a higher reflectance than measurement point 8. In Figure 21, the average reflectance spectrum can be seen for measurement points 3 and 5 and points 9 and 10. The reflectance for point 5 was higher than for measurement point 3. When looking closely at the images of the cartilage samples, it can be seen that measurement point 3 does have a small damage. The reflectance of point 10 was higher than for point 9.

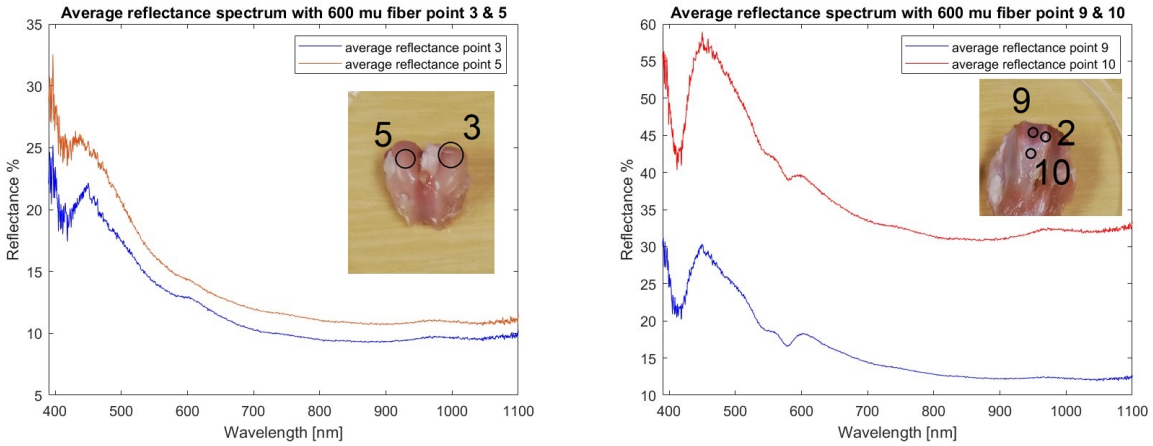

Figure 21: *The average reflectance spectrum for measurement points 3 and 5 using a 600 mu fiber (left) and the average reflectance spectrum for measurement points 9 and 10 using a 600 mu fiber (right).*

6.5 Discussion

The goal of this pilot study was to investigate the feasibility of the use of SFRS on cartilage. It can be seen in Figure 19 and 20 that the 300 mu fiber has a lower signal and overall has a lower reflectance than the 600 mu fiber does. A difference is visible between the reflectance of point 8 in comparison to point 7 (Figure 20). Point 7 differs from point 8 since point 8 lies on the right trochlear groove (where the patella normally lays in) and is often more damaged because of this. Besides, point 8 contains additional damage to the cartilage made by a hammer. The color from point 7 also differs from point 8 as point 7 is whiter. For both the 300 mu and 600 mu fiber point 7 had a higher reflectance. This is in accordance with the research conducted by K. van Assen [38], where cartilage samples with a higher macro score (worse quality) were found to have a lower diffuse reflectance as well. In Figure 21 it can be seen that point 9 had a lower average reflectance than point 10. Point 9 lies in the left trochlear groove, but no additional damage was created here. Point 3 also had a slight damage in the cartilage and when comparing those spectra to the spectra of point 5, the overall reflectance is indeed lower for the 600 mu fiber (Figure 21), but the differences are less evident.
It can be seen that measurements conducted with the 600 mu SFR fiber have a higher penetration depth since the absorption peaks of the hemoglobin (541 and 577 nm) are visible more clearly.
The accuracy and reliability of the measurements are low, as can be seen in Figure 19. Measurement 4 conducted with the 600 mu fiber deviates from the other measurements. This is partly because the measurements were conducted by hand-holding the fiber. Since the fiber tip is very small, the sample is slippery and the measurement fiber itself is flexible, it was difficult to remain at one point during the measurement. Another shortcoming is that measurements were conducted on rabbit cartilage (0.3 mm), which is thinner than human cartilage (2.2-2.5 mm). [47] For this reason, it is difficult to conclude from this study whether SFRS would be feasible for human cartilage as well.
Accuracy can be improved by using a microscope. The orientation of the fiber tip can be more easily observed using a microscope and this way, contact between the sample and surface of the fiber tip can be improved. To increase the stability of the fiber during the measurement, the fiber could be attached to a metal sheath (mimicking the Nanoscope sheath). This ensures that the fiber is less bendable making it easier to keep the fiber tip in one point.
Overall it can be said that in this pilot study distinguishment can be made between normal and damaged cartilage using SFRS, but reflectance is quite low and orientation of the fiber remains a challenge. Further research and more measurements are needed to draw conclusions on the extent of cartilage quality evaluation that can be done using SFRS.

7 Design

7.1 Design assignment

To test whether the expansion of needle arthroscopy with SFR spectroscopy improves the assessment of cartilage quality at an outpatient clinc, a prototype must be designed. By using the knowledge gained from literary research as well as discussion with various experts, hardware requirements for the design can be formulated. These hardware requirements can be subdivided into user, technical and functional requirements. The hardware requirements will be stated and explained in the sections below.

7.2 User requirements

- The product must enable the whole procedure to be carried out in under 45 minutes. [48]

  It must be intuitive and easy to conduct the spectroscopic measurement and interpret the results and therefore not take longer than current procedures using the Nanoscope. This is especially important since the product is used at an outpatient clinic. The product must fit into the current workflow of orthopedists.

- The product must not worsen the condition of the patient

  The product must merely function as a cartilage evaluation method.

7.3 Technical requirements

- The product must have a diameter smaller than or equal to 2.4 mm [23]

  The goal for the product is to be used at an outpatient clinic. Because it is known that the Nanoscope can be used under local Anesthesia, the product must have dimensions smaller than or equal to those of the Nanoscope.

- The product must not weigh more than 60 grams [49]

  The Nanoscope handpiece has a weight of 55 grams. Including the sheath and SFR fiber, should not increase the weight too much since this could hinder the workflow of the orthopedists.

- The surface of the fiber tip must be oriented flat to the surface of the cartilage.

  To gain the most reliable and accurate SFRS measurements, there should exist optimal contact between the surface of the fiber tip and the cartilage.

- The fiber tip must be visible by the Nanoscope imaging system

  To obtain optimal contact between the surface of the fiber tip and the surface of the cartilage, the fiber tip must be visible on the imaging system of the Nanoscope. This way the orientation of the fiber tip can be adjusted depending on the curvature of the articular cartilage and placement of the SFRS fiber can be more accurate.

- The product must not be able to rupture during the procedure

  It is important that the product can be moved around freely in the joint space without the risk of rupturing and losing materials in the joint space.

- The product must be fabricated of sterilizable materials

  To maintain patient safety and decrease the risk of infections caused by the procedure, materials must be sterilizable.

7.4 Functional requirements

- The product must be able to differentiate between healthy and degrees of degraded cartilage

  An accurate and reliable diagnosis is needed to be able to stop further progression of the disease.

- The product must be able to provide fluid flow during the procedure.

  Fluid flow is important for the visualization of the joint during the procedure when using the imaging sensor of the Nanoscope.

- Product must be able to conduct measurements on the central or weight-bearing regions of the articular cartilage surface

  The target group for the product is mainly patients suffering from isolated cartilage damage, which can be induced by injury and repetitive stress on a joint. For this reason, the product must target the regions of the articular cartilage which endure the most stress.

8 Discussion

Osteoarthritis is a prevalent articular cartilage disease with limited self-regeneration due to its aneural and avascular nature. Caused by aging and injury, it tends to progressively deteriorate. Early detection is crucial for prevention, as current techniques like MRI and arthroscopy are inadequate for early diagnosis. Needle arthroscopy is promising for cartilage evaluation at an outpatient clinic, and NIRS shows potential for quantitative assessment. This project focused on extending needle arthroscopy (specifically the Arthrex ®Nanoscope) with NIR spectroscopy. The aim was to formulate and evaluate hardware design requirements for this. The ultimate goal is to improve diagnostic capabilities for early osteoarthritis detection.
Through literature review and interviews with experts it was found that the current Nanoscope has limited space (0.5 mm in diameter) in the sheath for a spectroscopic device. Since the ultimate goal is to use the product at an outpatient clinic, it is of high importance that the diameter of the Nanoscope sheath is not enlarged. For this reason, SFRS considered a promising method for conducting spectroscopic measurements. From the pilot study conducted with SFRS, fibers it could be concluded that cartilage quality does affect the percentage reflectance of the light. Results showed that more damaged cartilage had a lower reflectance in comparison with 'healthy' cartilage. It could also be seen that differences in reflectance were more evident in the measurements conducted with the 600 mu fiber in comparison to the 300 mu fiber. These differences were greater in the visible wavelength range (380-700 nm) than in the VIS-NIR range (700-1100).
These results are promising for potential further research on the extension of the Nanoscope with SFRS. Since SFRS can be conducted using fibers with a smaller diameter than 0.5 mm, little to no adjustment of the dimensions of the Nanoscope device would have to be made.
Several limitations come with the results of this project. In the results of the pilot study, it can be seen that visible reflectance differences in the spectrum are the most evident in the wavelength region of visible light. Since the measurements were conducted using a VIS-NIR spectrometer, only a small part of the NIR wavelength range was examined in the study. This is a limitation since higher wavelengths in the NIR region contain a lot of information about the composition of cartilage (Chapter 4). In addition to that, the use of MDSFR (Chapter 5.2.5) has not been examined in this study, which could provide more info on cartilage quality. Because of the fact it uses multiple diameter fibers, it would be a challenge to implement this in the Nanoscope considering the dimensions of the sheath. A solution for this could be removing the Nanoscope from the sheath before inserting the SFR fibers. A big disadvantage of this is that placement of the fiber in a specific location would be very difficult and therefore it is not preferable. Another limitation of the use of SFRS for cartilage is the orientation of the fiber tip. To aqcuire reliable results, the contact between the fiber tip and cartilage surface must be optimal. To obtain this optimal contact between fiber tip and cartilage it must be taken into account that the fiber contains a polished angle and the cartilage sample contains a curvature as well. It is determined that the optimal polishing angle is 15 degrees. Because the Nanoscope is inserted sideways in the joint, a considerable physical angle must be obtained with the fiber.

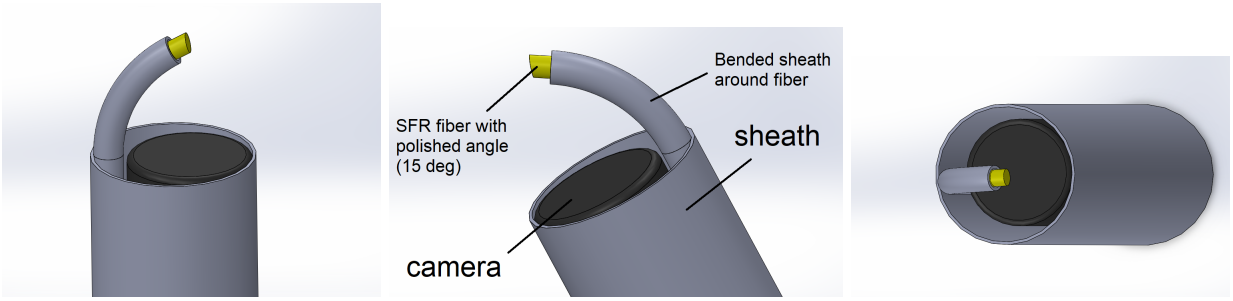

Figure 22: *Sketch of a possible solution for implementing SFR fiber in the Nanoscope sheath. In order to obtain optimal contact between the fiber tip and cartilage surface, fiber would make an approximate 75-degree physical angle. In addition, the fiber has an optimal polishing angle of 15 degrees. The fiber tip can be visualized by the camera for optimal placement of the fiber.*

A recommendation for further research is that the evaluation of cartilage quality using SFRS is further examined because the number of measurements obtained from this project is limited. It can not be concluded whether the use of wavelengths in the NIR region has added value in the evaluation of cartilage quality.

Overall, there is more data needed to draw a conclusion on the functionality of SFRS. It must also be investigated how and if quantitative distinguishment can be made between 'healthy' and 'degraded' cartilage using the same methods as described in Chapter 4.3. In addition to this, it must be studied to what extent MDSFR could improve cartilage quality evaluation using SFRS. Furthermore, more research is needed on how the orientation of the fiber tip toward the surface of the cartilage can be controlled and optimized while implemented in the Nanoscope. A sketch of a possible solution for this is shown in Figure 22. The sketch shows a combination of a polished angle of the fiber and a physical angle that the fiber makes, which can be visualized using the camera of the Nanoscope.

9 Conclusion

The aim of this project was to formulate and evaluate design requirements specifically for the extension of needle arthroscopy with Near-infrared spectroscopy. In this project, it was found that SFRS is a promising technique for conducting spectroscopic measurements through the Nanoscope needle arthroscopy device. During this project design requirements have been established in Chapter 7. It is important that the dimensions of the product are kept within the dimensions of the already existing Nanoscope needle arthroscope. Limitations of this project were the limited amount of data obtained from the pilot study and the fact that only the visible near-infrared wavelength region was included in the study. For the actual implementation of SFRS in the Nanoscope, the orientation of the fiber tip towards the surface of the cartilage remains challenging. For this reason, further research is needed on the functionality of SFRS in cartilage quality evaluation as well as the orientation of the fiber tip towards the cartilage.

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[49] Imaging and Resection.

A Appendices

A.1 Measurement results of pilot study

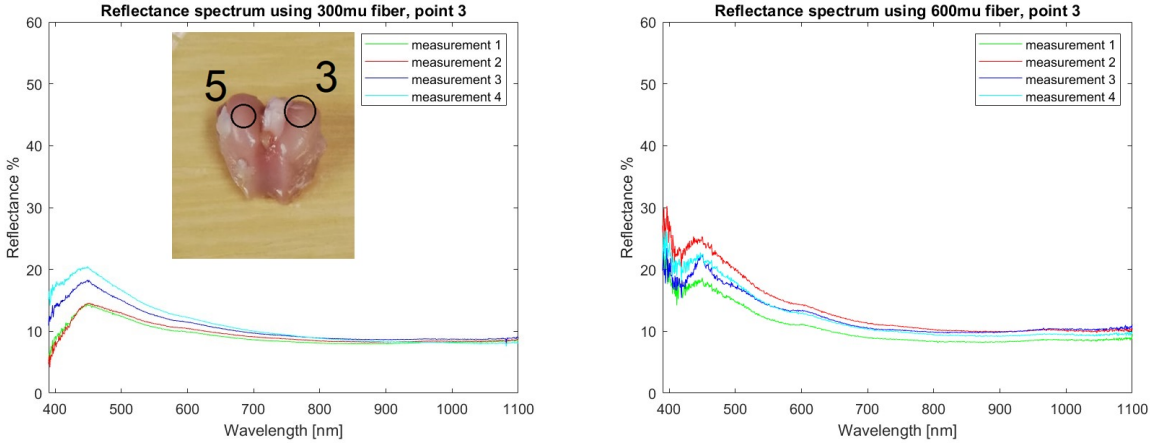

Figure A.1: *Reflectance of measurement point 3 with 300 and 600 mu fiber.*

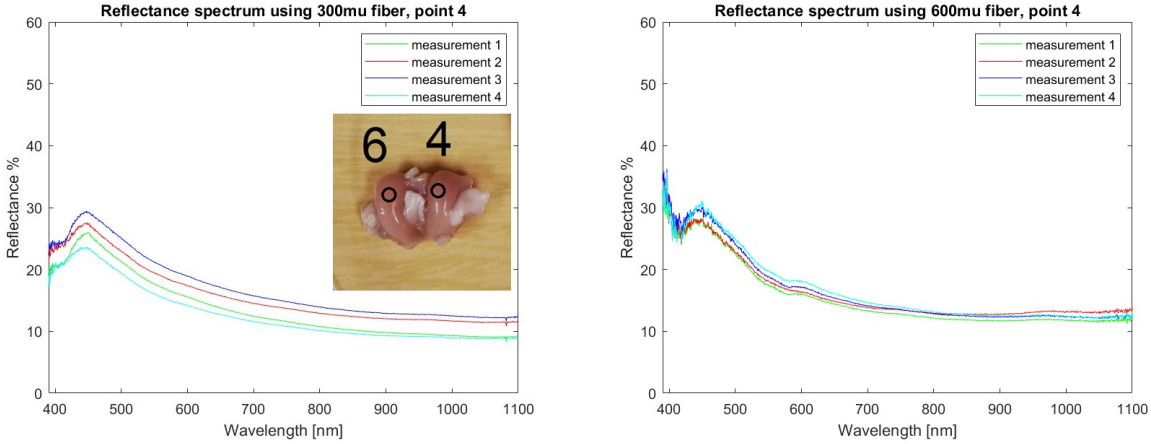

Figure A.2: *Reflectance of measurement point 4 with 300 and 600 mu fiber.*

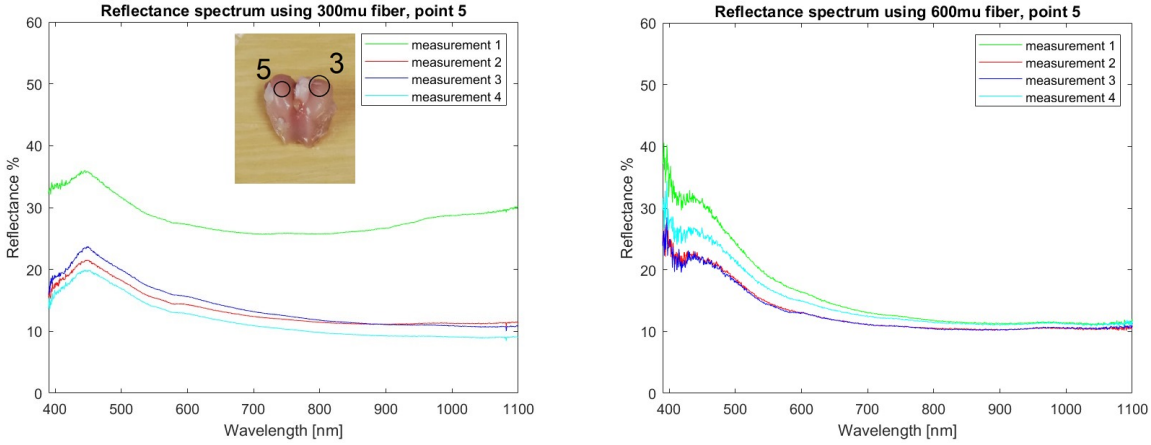

Figure A.3: *Reflectance of measurement point 5 with 300 and 600 mu fiber.*

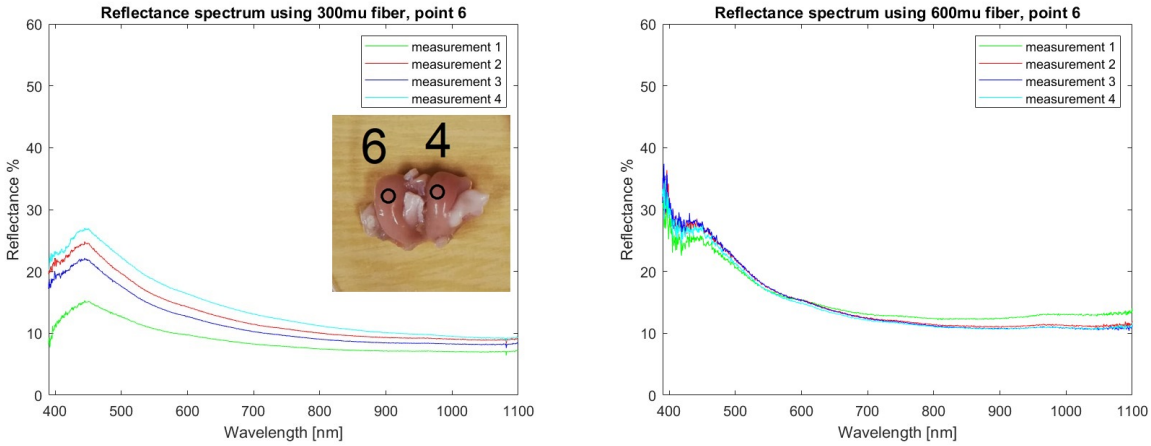

Figure A.4: *Reflectance of measurement point 6 with 300 and 600 mu fiber.*

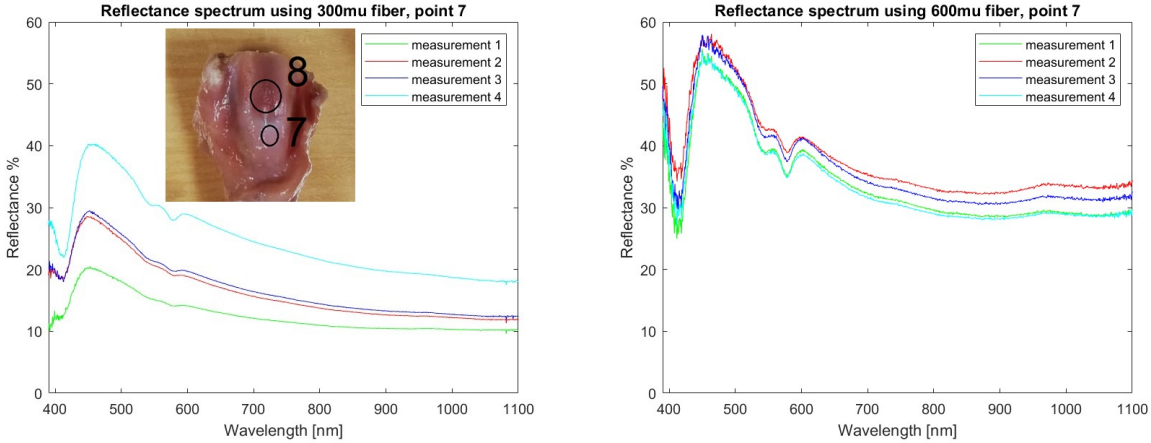

Figure A.5: *Reflectance of measurement point 7 with 300 and 600 mu fiber.*

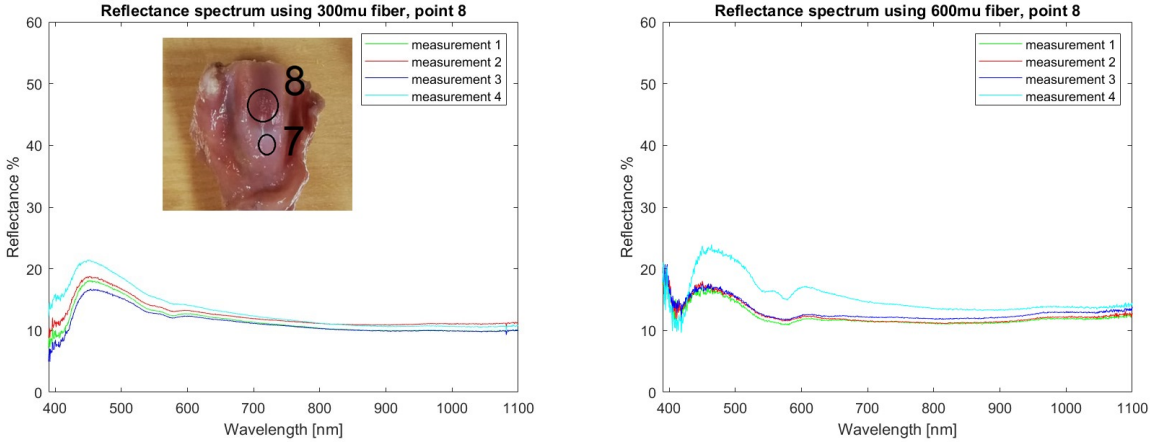

Figure A.6: *Reflectance of measurement point 8 with 300 and 600 mu fiber.*

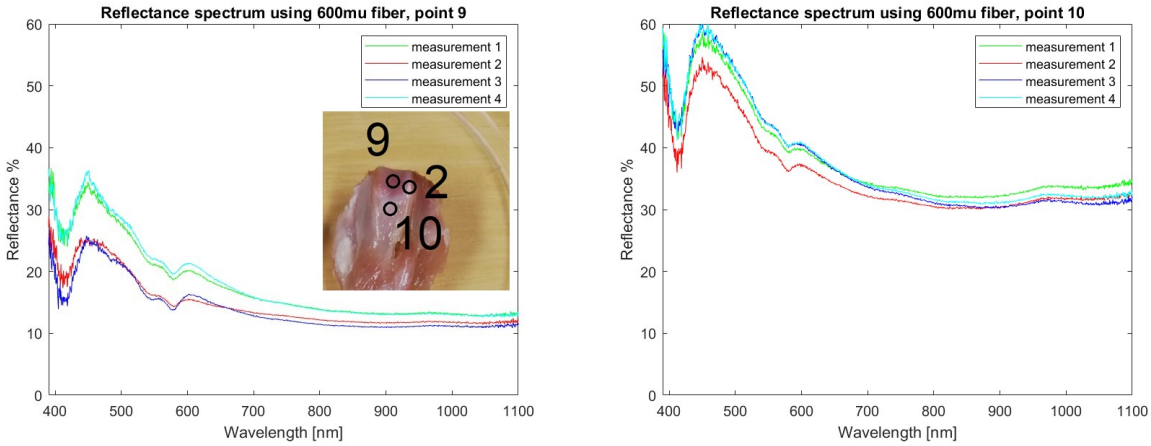

Figure A.7: *Reflectance of measurement points 9 & 10 with 600 mu fiber.*

A.2 Matlab script used for data analysis

```
%% Script for plotting different measurements of a single point.
close, clc

% Opening the Excel file containing data of spectrometer.
meting = readmatrix("600meting10.xlsx");
x = meting(:,1);
y1 = meting(:,2);                                   % Measurement 1
y2 = meting(:,3);                                   % Measurement 2
y3 = meting(:,4);                                   % Measurement 3
y4 = meting(:,5);                                   % Measurement 4


figure(1);
% Plotting the 4 measurements of the same point.
plot(x,y1,'g', x,y2, 'r', x,y3,'b',x,y4,'c');
xlim([390 1100])
ylim([0 60])
title('Reflectance spectrum using 600mu fiber, point 10')
xlabel('Wavelength [nm]')
ylabel('Reflectance %')
legend('measurement 1','measurement 2','measurement 3','measurement 4')

%figure(2);
%Y_avg = (y+y1+y2+y3)/4;

%% Script for plotting average measurements of different points

figure(2);
% Opening the Excel file containing data of the spectrometer
% of second measurement point.

meting2 = readmatrix("300meting5.xlsx");
x1 = meting2(:,1);
y5 = meting2(:,2);                                  % Measurement 1
y6 = meting2(:,3);                                  % Measurement 2
y7 = meting2(:,4);                                  % Measurement 3
y8 = meting2(:,5);                                  % Measurement 4

Y_avg = (y+y1+y2+y3)/4;
Y_avg2 = (y5+y6+y7+y8)/4;

% Plotting two average reflectance spectra in the same figure,
% from different measurement points.

plot(x, Y_avg, 'b', x1, Y_avg2);
xlim([390 1100])
ylim([10 60])
title('Average reflectance spectrum with 300 mu fiber point 3 & 5')
xlabel('Wavelength [nm]')
ylabel('Reflectance %')
legend('average reflectance point 3', 'average reflectance point 5')
```