Saggital optical tomography for the diagnosis of rheumatoid arthritis in finger joints

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Abstract: Inflammatory processes as they occur during rheumatoid arthritis (RA) lead already in early stages of the disease to changes in the optical properties of joint tissues and fluids. In this work we report on in vivo studies involving human subjects, which show the potential of optical tomographic techniques for the early diagnosis of RA.

OCIS codes: (170.0170) Medical optics and biotechnology, (170.4580) Optical diagnostics for medicine

1. Introduction

Rheumatoid arthritis (RA) is a chronic, progressive, inflammatory disease that primarily attacks peripheral joints and surrounding tendons and ligament.[1] This disease, which is often associated with significant pain and disability, affects approximately 2.1 million people in the US.[2,3] RA is characterized by an inflammatory synovitis that leads to cartilage and bone destruction and consequent loss of function. The synovial tissue becomes infiltrated with inflammatory cells and activated, invasive fibroblast-like cells, which may invade bone and cartilage. In general, 4 different disease stages can be distinguished, during which the tissue change is gradually.[4,5] During stage 1 (Synovitis) inflammation leads to edema in the synovial membrane (synovium) and joint capsule. The permeability of the synovium is changed leading to an increase of fluid and large cells in the synovial cavity. In stage 2 (Pannus) a thickened layers of granulation tissue covers and invades the articular cartilage. The joint cartilage and adjacent bone are destroyed. In stage 3 (Fibrous Ankylosis) an invasion of the pannus with scar tissue occurs, which closes the joint space. Muscle and bone undergo atrophy and misalign, leading to subluxation and visible deformity. Finally in stage 4 (Bony ankylosis) fibrous tissue calcifies and leads to immobility of the joint. In recent years the importance of the early pathophysiological stages has been increasingly recognized and led to other definitions of the stages.[6]

Imaging of the joint has so far only played a role in later stages of the disease. Radiography can document the bone damage that results from RA and visualize the narrowing of cartilage spaces. However, it has long been recognized that radiography is insensitive to the early manifestations of rheumatoid arthritis. Optical techniques promise to provide a new tool for the early detection of RA. Changes of the optical properties of the synovium and the synovial fluid can be observed already in the very early stages of the disease. For example, the normally clear yellowish synovial fluid turns into a turbid grayish substance.[7]

The goal of this work is to go beyond numerical studies [89] and to perform initial clinical studies on human subjects with RA to demonstrate the feasibility of optical techniques to detect the changes in optical properties inside the interphalangeal PIP joint. We present tarnsillumination data as well reconstructed images that show the optical properties in a saggital plane through the finger. The reconstruction algorithm is based on model-based iterative image reconstruction (MOBIIR) scheme,[10] which uses the equation of radiative transfer as a forward model of light propagation.[11] An adjoint differentiation technique is employed to calculate the gradient calculation of the objective function with respect to the spatial distribution of optical properties.[12,13]

2. Methods

For the diagnosis of rheumatoid arthritis it is of particular importance to determine the changes in the optical properties of the synovial fluid and the synovium. These changes are dominated by changes in the scattering coefficient. To obtain these optical properties one cannot rely on dynamic changes, but needs to reconstruct absolute values. Dynamic changes may have their own diagnostic value, as discussed in a separate paper in this proceedings by Lasker et al.[14]. In this work we concentrate on measuring absolute tissue optical properties. To this end we have developed a device that allows for measuring with high accuracy the transmission profiles. A

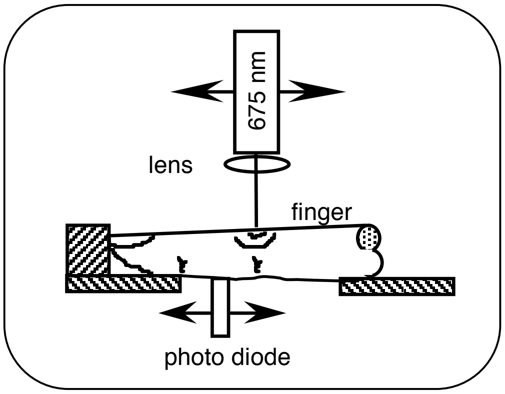

Fig.1 Experimental setup for saggital finger joint

scheme of the device is shown in Fig. 1. A laser diode and a Si-photodiode are independently scanned over a distance of up to 3 cm along the saggital plane across the joint. The photodiode is in direct contact with the finger, while the beam of the laser diode is focused to a spot of approximately 0.3 mm in diameter on the back of the finger. During a measurement, the laser diode is first brought to the desired position on the back on the finger. The photodiode is then scanned over a distance of 3 cm and the transmitted intensities are detected. After the detector scan is finished, the laser diode is moved by a distance of Δx, and the photo-diode performs another scan, etc.. In this way several transmission profiles like in Fig. 2 are obtained. Since no optical fibers are used and the same source and detector are employed for each measurement, the recorded profiles can be directly compared to each other without additional calibrations for fiber incoupling losses, different source strengths, or detector sensitivities.

The measured data is then input to a model-based iterative image reconstruction scheme, which uses the equation of radiative transfer as a forward model. The use of the diffusion approximation (DA) as a forward model is not appropriate in this case, since it has been shown that the DA fails to accurately describe light transport in void-like areas, such as the synovial-fluid-filled space inside the joint. An initial guess of the distribution of optical properties is input to the forward model, which generates a prediction of the expected measurement data. The objective function that compares the predicted data and the actually measured data is defined as the normalized least square error between the data sets. An adjoint differentiation algorithm is then used to determine the gradient of the objective function. This gradient is used to determine a search directions for the iteration within the MOBIIR code. More detailes concerning this algorithm can be found elsewhere.[11-13]

A total of 8 volunteers with RA in stage II were recruited and informed consent was obtained prior to the study. All of the subjects were diagnosed with RA in at least on of the interphalangeal PIP joint of one hand, while the same joint in the contra-lateral hand was found to be not affected. Inflamed blood was present, but no bone or cartilage damage was visible on radiographs. The examined fingers showed no outside swelling or nodules. Optical trans-illumination measurements were performed on the same joint of both hands.

3. Results

In all cases we found significant differences in the saggital trans-illumination data between the healthy joint and the joint with symptoms of RA. An example of a set of measurements from a subject is shown in Figs. 1a and b. In both figures trans-illumination curves for 5 different source positions, which are indicated by the arrows, are shown. Source position 2 is closes to the finger tip, while source position 18 is furthest from the finger tip. In Fig. 2a, which illustrates a measurement on a healthy joint, the trans-illumination data for the source #10, clearly shows the strongest transmission signal with a maximal amplitude at least 1.5 as strong as any other measurement with a different source position. This is expected since source position 10 is located directly on top of the joint, which is filled with relatively low scattering and low absorbing synovial fluid. In Fig. 2b, which shows measurements on a rheumatoid joint, measurements at source position #10 don't show such a strong signal. Here the strongest signal is measured for the source position closest to the finger tip, were the finger diameter is smallest. As the source is moved further away from the fingertip, the signal gets progressively smaller.

Fig. 3 shows the reconstructed cross-section of the scattering coefficient in the saggital plane of the healthy joint. For this reconstruction trans-illumination data from additional source position, not shown in Figs. 1, were also included. The finger tip is located to the left of the images which shows a 3-cm-wide saggital section of the finger, with the joint located in the center. The reconstruction was started with an initial guess of ${}_s$= 100 cm^{-1}, and ${}_a$ = 0.5 cm^{-1}. The anisotropy factor g was fixed at 0.9. While the spatial resolution is poor, clearly visible is the drop of the value of the optical properties around teh location of the joint, which is filled with the low scattering and low absorbing synovial fluid. In the reconstructions on the joints affected with RA, this drop is not visible.

These results clearly show the potential of optical techniques to diagnose RA in its early stages. To fully explore this potential, we are currently pursuing studies to quantify the sensitiviry of optical tomographic techniques to changes in the optical properties of the synovial fluid. Initial results indicate that using OT techniques difference as small as 15% can be detected. Further clinical studies need to be performed to fully explore the diagnostic potential of optical tomographic techniques for RA.

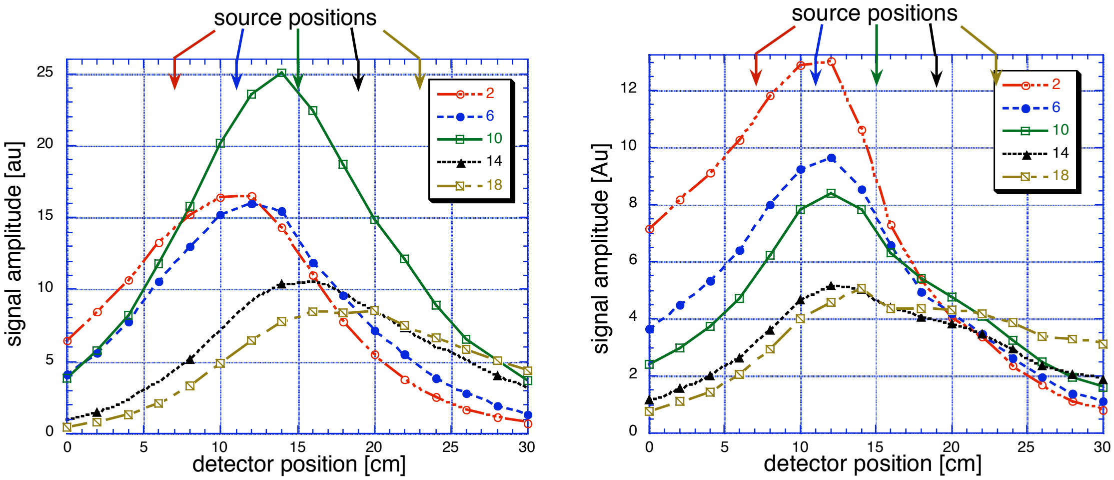

Fig. 2 Intensity transmission profiles for 5 different source positions for a healthy joint (left) and the same joint on the contra lateral hand with with rheumatoid arthritis (rigth). Source position 2 is closes to the finger tip, while source position 18 is furthest from the finger tip. Source position #10 is located directly above the PIP joint.

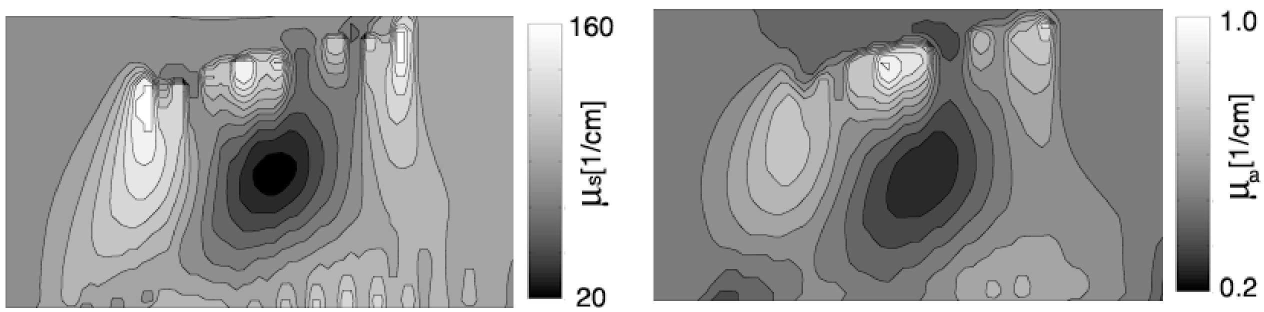

Fig. 3. Reconstructed cross-section of the scattering coefficient (left) and absorption coefficient (right) in the saggital plane through the healthy joint.

5. References

[1] J. Norris, Senior Editor, *Professional guide to diseases*, 5th Edition, Springhouse Corp., . Springhouse, PA, 1998, pp. 355-360.

[2] E.D.J. Harris, "Rheumatoid arthritis: Pathophysiology and implications for therapy," *N. Engl. J. Med.* 322, 1277- , 1990.

[3] D. P. Lubeck, "The economic impact of arthritis," *Arthritis Care and Research* 8, 304-310 (1995).

[4] P.F. Laudicina, Applied Pathology for Radiographers, (Philadelphia, PA: W.B. Saunders Company, 1989) p. 147

[5] O. Steinbrocker, C.H. Traeger, R.C. Batermann, "Therapeutic criteria in rheumatoid arthritis,"*J. Amer. Med. Ass.* 140 (8), pp. 659-xx (1949).

[6] E. D. Harris, "Rheumatoid Arthritis: Pathophysiology and Implications for Therapy," *The New England Journal of Medicine* 322, 1277-1289 (1990).

[7] J. Beuthan, V. Prapavat, R.-D. Naber, O. Minet, and G. Müller, "Diagnosis of inflammatory rheumatic diseases with photon density waves," Proc. SPIE Int. Soc. Opt. Eng. **2676**, *Biomedical Sensing, Imaging, and Tracking Technologies I*, R. A. Lieberman, H. Podbielska, T. Vo-Dinh, eds., 43-53 (1996).

[8] A. Klose, V. Prapavat, O. Minet, J. Beuthan, and G. Mueller, "RA diagnostics applying optical tomography in frequency-domain," Proc. SPIE Int. Soc. Opt. Eng. **3196**, 194-204 (1997).

[9] A. D. Klose, A. H. Hielscher, K. M. Hanson, and J. Beuthan, "Three-dimensional optical tomography of a finger joint model for diagnostic of rheumatoid arthritis," Proc. SPIE Int. Soc. Opt. Eng. **3566**, 151-160 (1998).

[10] A.H. Hielscher, A.D. Klose, K.M. Hanson, "Gradient-based iterative image reconstruction scheme for time-resolved optical tomography," *IEEE Transactions on Medical Imaging* **18**, 262-271 (1999).

[11] A.D. Klose, U. Netz, J. Beuthan, A.H. Hielscher, "Optical tomography using the time-independent equation of radiative transfer. Part 1: Forward model," *Journal of Quantitative Spectroscopy and Radiative Transfer*, in press.

[12] A.D. Klose and A.H. Hielscher, "Iterative reconstruction scheme for optical tomography based on the equation of radiative transfer," *Medical Physics* **26** (8), 1698-1707 (1999).

[13] A.D. Klose, A.H. Hielscher, "Optical tomography using the time-independent equation of radiative transfer. Part 2: Inverse model," *Journal of Quantitative Spectroscopy and Radiative Transfer*, in press.

[14] J.M. Lasker, A.Blustone, C. Schmitz, R.L. Barbour, and A.H. Hielscher, "Volumetric optical-tomographic dynamic imaging of small tissue volumes," Technic Digest of Biomedical Topical Meeting on Advances in Optical Imaging and Photon Migration 2002.

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