Journal of Biomedical Optics

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Abstract. A photoacoustic (PA) and ultrasound (US) dual modality system, for imaging human peripheral joints, is introduced. The system utilizes a commercial US unit for both US control imaging and PA signal acquisition. Preliminary *in vivo* evaluation of the system, on normal volunteers, revealed that this system can recover both the structural and functional information of intra- and extra-articular tissues. Confirmed by the control US images, the system, on the PA mode, can differentiate tendon from surrounding soft tissue based on the endogenous optical contrast. Presenting both morphological and pathological information in joint, this system holds promise for diagnosis and characterization of inflammatory joint diseases such as rheumatoid arthritis. [DOI: 10.1117/1.JBO.18.1.010502]

Keywords: medical and biological imaging; medical optics instrumentation; photoacoustic imaging; ultrasound.

Paper 12589L received Sep. 6, 2012; revised manuscript received Nov. 20, 2012; accepted for publication Nov. 26, 2012; published online Dec. 12, 2012.

Rheumatoid arthritis (RA) is a leading cause of disability in the United States. This disorder affects one to three percent of the U.S. population. Inflammation of peripheral joints is an early sign in RA and precedes irreversible structural damage.[1] The evaluation of human finger joints is, therefore, essential for diagnostic imaging and to monitor response to treatment in RA and other rheumatologic conditions including seronegative spondyloarthropathies, systemic lupus, crystal deposition diseases and osteoarthritis. Although radiography has, for decades, been the gold standard for the detection and assessment of musculoskeletal diseases, it is invasive radiation and inability to characterize early soft tissue changes prompts the need for novel imaging modalities that are noninvasive, nonionizing, and have better sensitivity to soft tissue pathological changes.

Pioneering studies, implementing diffuse optical tomography (DOT) of human peripheral joints, have demonstrated desirable imaging depth and sensitivity to physiological changes associated with RA and osteoarthritis.[2–4] The spatial resolution of DOT, however, is limited by it's dependence on diffused photons as detection signals. Integrating the structural information extracted from secondary imaging modalities, such as US, can improve the image quality of DOT.[5,6] Yet, the compensation regime could be less effective if the distribution of optical properties does not coincide with that of acoustic impedance in the first place. As an emerging technology, PA imaging physically combines the optical and ultrasonic waves by detecting the ultrasonic signals generated by laser-induced thermoelastic expansion within biological tissue. The imaging modality, thereby, inherits the merits of pure optical tomography while attaining the spatial resolution comparable to high frequency US imaging. *Ex vivo* studies in the rat tail and human finger joints and an *in vivo* study in osteoarthritis demonstrated the capability of PA imaging in achieving submillimeter resolution and identifying optical properties in articular tissues and variations induced by inflammation.[7–10] However, utilizing single or limited number of transducer elements and home-fabricated sophisticated devices for signal acquisition, as in most current PA imaging systems, undermines the system compactness and imaging speed as well as repeatability of imaging findings which drastically hinders quick adaptation of novel photoacoustic tomography (PAT) techniques to clinical settings.[4,7,9]

Achieving new PA imaging functions, through a commercial US unit, could accelerate the clinical acceptance of novel PAT techniques.[11–14] With potential dual-modality arrangement, US and PA images of a target tissue can be scanned with the same system, generally along the same view angle with, essentially, the same refraction errors which results in naturally co-registered images. In comparison with PAT, US is a more established imaging modality. Images from US could be used to guide the PA imaging procedure and help interpret novel PAT findings. PAT results can also be more easily reproduced between laboratories. Moreover, by combining with a production medical US system, the development of PA imaging can be accelerated by taking advantage of the state-of-the-art US technologies such as large number of parallel channels each with commercial grade receiver sensitivity and noise characteristics.[15,16] In this study, a dual modal system facilitating both US and PA imaging for clinical study on human inflammatory arthritis is presented. Through preliminary experiments on human finger joints, the system, in noninvasive imaging of peripheral joints and presenting both ultrasonic and optical contrasts, has been validated.

Figure 1 shows the schematics of the system. The system integrates a tunable optical parametric oscillator (OPO) laser (Vibrant B, Opotek Inc, Carlsbad, California) pumped by the second harmonic output of an Nd:YAG pulsed laser (Brilliant B, Quantel, Bozeman, Montana) as the illumination source. The laser system is tuned to 740 nm which gives the maximum output energy of 80 mJ per pulse. The laser pulses, with a repetition rate of 10 Hz and pulse width of 5.5 ns, are coupled into an optical fiber bundle (CeramOptec Industries Inc, East Longmeadow, Massachusetts) which consists of 18 fibers fused together at the input end for best coupling of light energy. As shown in Fig. 2, the fibers, at the output end of the bundle, are arranged into four linear arrays which bilaterally illuminate the finger horizontally rested on the imaging platform [marked with the blue lines in Fig. 2(a)]. Considering the coupling efficiency of 30 to 40 percent of the fiber bundle (approximately 30 mJ per pulse delivered to

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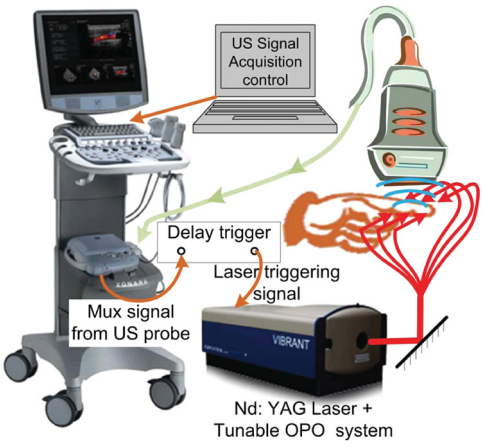

Fig. 1 Schematic of the US/PA dual modality imaging system for human peripheral joints.

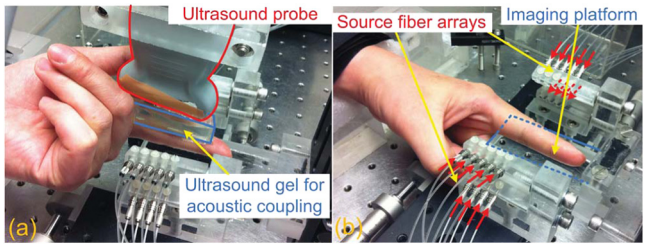

Fig. 2 The experiment setup. (a) Imaging scheme for coronal middle plane from the volar side; (b) Imaging scheme for sagittal middle plane. The US transducer is removed to better display the fiber optics arrangement.

the finger) as well as the beam spreading before light reaching the target finger, the light energy density, on the skin surface, is approximately 4 mJ · cm^{-2} which is significantly lower than the ANSI safety limit. A commercial US unit (Z.ONE, ZONARE Inc.) is used to acquire the PA signals. A linear array (L10-5, ZONARE Inc.), with a working band of 5 to 10 MHz [delineated with red curves in Fig. 2(a)], is positioned perpendicular to the imaging platform and coupled to the finger surface with a block of agarose gel, as delineated with the blue lines in Fig. 2(b). The lateral resolution, of the PAT system, in the focal plane is approximately 300 μm at a distance of 20 mm from the probe surface. For each finger joint, both the volar side of the coronal [as shown in Fig. 2(a)] and the sagittal [as shown in Fig. 2(b)] middle planes are scanned. The scanning plane, for PA imaging of a human finger joint, corresponds to that of standard ultrasound evaluation in clinical practice.

Before the acquisition of a PA image, a gray scale US imaging of the same joint along the same view angle is conducted which guarantees that the PA image be acquired along a desirable plane in the joint for best visualization of articular structures. Since the Z.ONE US system only possesses 64 receiving channels, whereas, the transducer array includes 128 elements, the data acquisition is split into two cycles each serving 64 channels. To achieve better signal-to-noise ratio, signal averaging over 90 laser pulses is performed. Therefore, the data acquisition, for a 2D B-scan image, takes approximately 1 min which could be substantially reduced in future clinical applications by employing an US unit facilitating 128 channels and a more powerful laser enabling higher pulse repetition rate with sufficient energy for each pulse. The time gain compensation of 60 dB is applied during both US and PA signal acquisition.

The system performance was preliminarily evaluated by a healthy volunteer pool comprised of five males and one female. The volunteers have no history of rheumatologic conditions or clinical evidence of peripheral joint involvement. The fingers of the subjects are fixed to avoid the motion artifacts in the PAT images. This study was approved by the Institutional Review Board of the University of Michigan Medical School and all subjects provided written informed consent. Figure 3 shows the example images acquired from a healthy male and a healthy female subject, respectively. The images were reconstructed using a back-projection algorithm with a fixed transducer F-number of one. The reconstruction algorithm assumes homogeneous light fluence distribution in the imaging plane, which is reasonable considering the bilateral illumination regime and good penetration of near infrared (NIR) light in the small peripheral joints of human fingers. Although the osseous structures in the finger joint could cause acoustic reflection and reverberation, the reconstructed tissue features above the bone surfaces are reliable.

The comparison between PA and US images, of the proximal interphalangeal (PIP) joints of normal volunteers shown in Fig. 3, demonstrates prominent similarities between the osseous structures in PAT and in US, as well as tendon and cartilage. However, the image contrasts are fundamentally different in that US images represent the acoustic reflection of the osseous structures, while PA images most likely represent the optical energy absorption of the vasculature in the periosteum on the bone surfaces. The delineation of the borders between the surrounding soft tissue and tendon in US images is based on the different echogenicity, whereas, the optical contrast between the tendon and other soft tissues is originated from the different blood contents in various tissues. This partially substantiated our hypothesis that PAT, when integrated with a commercial US unit, can better identify functional characteristics, including both lood content and blood oxygen saturation, in articular tissues for improved diagnosis of inflammatory joint diseases. Although the strongest PA signals are originated from the bone surfaces in healthy PIP joints, it is expected that high optical absorption contrast could be detected in or around inflamed joints. To our knowledge, this is the first time the distinctive appearance of tendon by PAT has been presented. This is probably due to the high frequency commercial US transducer that produces high resolution imaging co-registering US and PA images.

PA and US images, from the same joints, show comparable spatial resolution. We also notice that the contours of the bones and tendons, in PA images, are not as distinct as those in US images which is partially due to the relatively low signal-to-noise-ratio of PA signals. Another reason is that the sophisticated US signal and image processing techniques facilitated by the commercial US unit, such as postreconstruction high-pass filtering, have not been involved in the PA image reconstruction. On the other hand, the imaging depths, presented by the PA and US images, are similar with both rendering the tissue structures above the bones very well while not many features below the bone surfaces are presented due to the blockage of ultrasound waves. This also suggests that the optical penetration, in the NIR region, is sufficient for a B-scan imaging of a human finger joint with PAT. Synovial tissue in the joint is primarily inflamed in inflammatory arthritis. Early changes of inflammation include neovascularization and migration and pooling of blood and

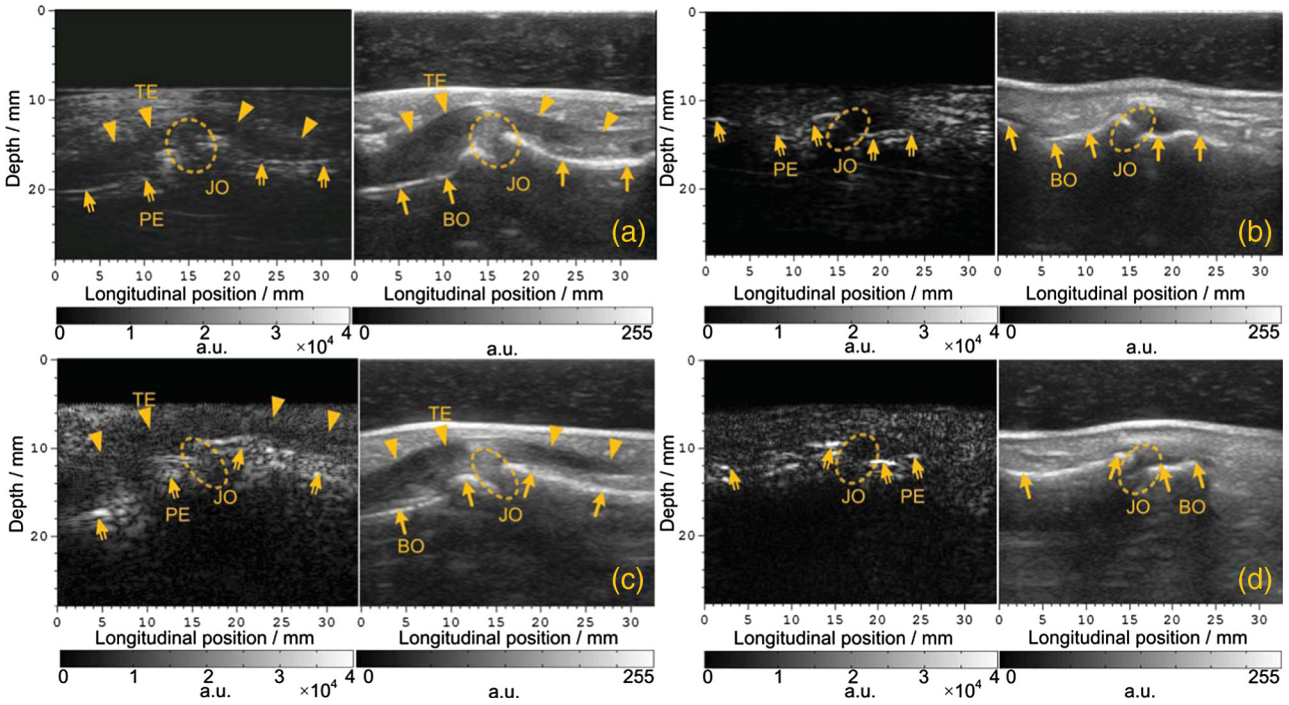

Fig. 3 PA (left in each subfigure) and US (right in each subfigure) images acquired from healthy volunteers. (a) Coronal plane [volar] and (b) sagittal plane images acquired from the PIP joint of an index finger of a male volunteer; (c) Coronal plane [volar] and (d) sagittal plane images acquired from the PIP joint of an index finger of a female volunteer. TE: tendon, JO: joint, PE: periosteum, BO: bone.

blood products. PA imaging is more sensitive than ultrasound when detecting blood volume and, unlike ultrasound, is not limited by the absence of flow.

This study introduces a PA and US dual-modality imaging system, built on a commercial US unit, for imaging of human peripheral joints. The preliminary *in vivo* evaluations, with health human finger joints, indicated that the system could recover comparable structural features in a joint with two different contrasts (ultrasonic and optical). The system also, for the first time, demonstrated distinctive appearance of tendon when compared to the surrounding soft tissue primarily based on the blood content. As the next step, to assess the value of this technique in clinical evaluation of inflammatory joint diseases, this system will be implemented to the human joints affected by RA. It is expected, that the structural resolving power of the system may facilitate reliable detection and quantification of the morphological markers of RA including bone erosions, joint space narrowing, synovial edema, andothers. Simultaneously, the functional contrast, produced by physiological markers including neoangiogenesis, hyperemia and hypoxia, may also be closely monitored. The authors also consider improving the imaging geometry by integrating the illumination fibers to the US transducer so that a handheld probe, which enables PA imaging, can be adapted to any peripheral joints conveniently.

Acknowledgments

This work was supported by the National Institutes of Health (NIH) under Grant Number R01AR060350 and R01AR055179.

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