The evolution of ultrasound in rheumatology

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Abstract: Musculoskeletal ultrasound is a powerful tool not only for evaluating joint and related structures but also for assessing disease activity. Ultrasound in rheumatology has rapidly evolved and been incorporated into routine clinical practice over the past decade. Moreover, technological development of equipment has made it more accessible for rheumatologists. We present a review of advances in ultrasound in rheumatology, focusing on major chronological developments.

Keywords: evolution, musculoskeletal ultrasound, rheumatology ultrasonography

Introduction

Musculoskeletal ultrasound has been considered a diagnostic tool for a variety of rheumatologic diseases for more than 30 years. However, its use has increased dramatically over the past decade, largely as a result of technological developments and falling costs. The former has allowed the production of high-quality and more easily interpretable images and the latter has made machines more affordable and accessible to the clinician. These improvements have been influential in driving the interests of the rheumatologist, particularly with respect to inflammatory arthritis and the early identification of inflammation and structural damage. In this review, we explore the major chronological advances of musculoskeletal ultrasound and highlight potential future directions in rheumatology.

Brief history: from the discovery of ultrasound to recent high-end machines

In the history of the development of ultrasonography, one of the most important contributions is certainly from Lazzaro Spallanzani, an Italian biologist, who observed, in the eighteenth century, that blindfolded bats were able to avoid thin wires stretched across a dark room. This ability was prevented when wax was placed in the bats' ears, and not when they were blindfolded, so that he concluded that their capacity to 'see' was strictly dependent on their ears. However, he was unaware that the bats used ultrasound to avoid the wires.

In 1843, the Austrian astronomer, physicist and mathematician Christian Doppler described the apparent change in frequency and wavelength of a mechanical wave perceived by an observer when the source of sound moved in relation to the object. This effect, later coined the 'Doppler effect', is the principle of the technique for estimating synovial blood flow in rheumatology ultrasound assessment. However, it was not until 1880, through the discovery of the piezo-electric effect of crystals by the French physicist Curie brothers, that the first relevant step to the development of modern ultrasound probes was made. The first realization of the use of ultrasound began in the military sector with the development of sound navigation and ranging (SONAR) systems for submarines during the First World War. Subsequently, its first development as a medical diagnostic tool is attributed to the Austrian neurologist Karl Dussik who in 1942 described his attempt to identify the cerebral ventricles and brain tumours using ultrasound beams directed through the skull [Dussik, 1942]. Shortly afterwards, Scottish obstetrician Ian Donald and Glasgow engineer Tom Brown developed the first A-mode a unidimensional ultrasound scanner and investigated abdominal masses [Donald *et al.* 1958].

The first clinically relevant musculoskeletal ultrasound study was published in 1972, in the *British Journal of Radiology*, by American radiologists Daniel McDonald and George Leopold [McDonald and Leopold, 1972]. They described the use of a contact B-mode, real-time scanner to

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differentiate Baker's cysts from thrombophlebitis. Six years later, in 1978, using greyscale ultrasound, a Canadian radiologist Peter Cooperberg published the first demonstration of synovitis in patients with rheumatoid arthritis [Cooperberg *et al.* 1978]. Since then, ultrasound has gained an increasing interest from musculoskeletal practitioners as it allowed the potential to directly visualize the primary site of pathology and a better understanding of joint pathophysiology. In recent years, increasing and changing demands made by the clinicians have influenced the direction of ultrasound development by manufacturers.

Nowadays, the cost of ultrasound equipment is quite variable. Equipment providing the highest image quality and the larger range of software add-ons is more expensive. However, the less expensive and less sophisticated units have facilitated the diffusion and accessibility of ultrasound training to a larger number of rheumatologists. Touch and flat screens of the latest-generation machines mean the traditional keyboard is no longer required which is relevant to the miniaturization of the machine; these screens also allow an easier and quicker transition between different aspects of the ultrasound examination. The feasibility to transfer small ultrasound equipment easily between different rooms of the same institution is also an advance. In addition, smaller and higher frequency transducers have facilitated the improved visualization of superficial and tiny anatomical structures such as ligaments, tendons and smaller joints. Despite the availability of different types of transducers, linear probes are best able to assess all indications in musculoskeletal ultrasound. The development of the 'hockey stick' probes, so called because of their shape, has surely facilitated the evaluation of joints that are difficult to reach due to their anatomy and size. Moreover, the use of small and handy probes has enabled the operator to obtain better angulation and control, thus reducing the risk of creating image artefacts.

From the first demonstration of synovial thickening to the end of the twentieth century

After the first greyscale demonstration of synovial thickening pre and post treatment with yttrium-90 injection in rheumatoid arthritis of the knee using 5 MHz of ultrasound frequency in 1978 [Cooperberg *et al.* 1978], interest in imaging smaller joints and periarticular structures has grown amongst clinicians. Three years

later, in 1981, the first report on the utility of ultrasound to successfully guide a joint aspiration in a patient with advanced rheumatoid arthritis with bilateral shoulder dislocation due to septic arthritis was published [Gompels and Darlington, 1981]. In 1988, the first ultrasound description of rheumatoid nodule and tenosynovitis in patients with rheumatoid arthritis was detailed [De Flaviis *et al.* 1988].

On the basis of these publications, in the late 1980s, a small group of enthusiastic European rheumatologists started to practice musculoskeletal ultrasound and published pioneering articles on the use of the technique in rheumatology clinics [Koski, 1989; Koski *et al.* 1989; Iagnocco *et al.* 1992]. Koski and colleagues demonstrated intra-articular effusion or synovitis in clinically and radiologically apparently normal hip joints of patients with active rheumatoid arthritis [Koski, 1989] and Iagnocco and colleagues found that cartilage thickness measured with a 5 MHz linear probe was diminished both in rheumatoid arthritis and in osteoarthritis knees compared with normal joints [Iagnocco *et al.* 1992]. In these studies, only greyscale ultrasonography in which images are produced in a black and white format was used.

In 1994, the first paper demonstrating the ability of power Doppler to visualize abnormal joint vascularity was published and this subsequently led the way for modern rheumatology ultrasound practice [Newman *et al.* 1994]. In the following year, the first use of colour Doppler ultrasound to diagnose temporal arteritis was published by pioneering rheumatologists in this field [Schmidt *et al.* 1995]. Since then, ultrasound for vasculitis of both small and large vessels started to attract rheumatologists' interest [Hau *et al.* 1999].

Towards the end of 2000, the recognition of the potential of ultrasound as a method to confirm the primary diagnosis and to assess therapeutic response in many rheumatologic diseases spurred the interest of rheumatologists to learn the technique themselves in order to improve their clinical practice. To support the learning needs of rheumatologists a 'EULAR [European League Against Rheumatism] Working Group for Musculoskeletal Ultrasound' was formed by rheumatology experts in 1998. Thus, the first EULAR ultrasound training course entitled 'An introduction to musculoskeletal ultrasound' was held in the Netherlands in 1998 [Wakefield *et al.* 1999].

The twenty-first century has opened a new era for ultrasound in rheumatology

As more rheumatologists have begun to learn ultrasound, structured training programmes have needed to be developed and researches have progressed towards more specific focuses in the twenty-first century.

Developments in education and training

To accommodate increasing numbers of learners and their requirements, in 2006, EULAR started to divide the EULAR ultrasound course into different levels by launching the first advanced ultrasound course in Denmark for experienced rheumatologists. In the following year, the members who organized the 14th EULAR ultrasound courses in 2007 developed the educational guidelines for the contents and conduct of future EULAR ultrasound courses, which proposed an educational model with three levels of basic, intermediate and advanced [Naredo *et al.* 2008]. The educational model has been successfully applied to the EULAR ultrasound course. As education progresses towards more structured outcomes, the need for competency assessment reflecting practical skills, knowledge and personal qualities has increased. Currently, an assessment and quality assurance process for trainees has been suggested for development by the EULAR Standing Committee for Education and Training; however, there is still a lack of consensus regarding how to determine whether trainees have enough theoretical knowledge and practical skills.

As in Europe, the use of musculoskeletal ultrasound by rheumatologists has also grown steadily in America. An ultrasound workshop has run at the American College of Rheumatology (ACR) since 1999, but it was not until 2005 when a focus group known as USSONAR (Ultrasound Society of North American Rheumatologists) was formed to foster training and research in ultrasound by rheumatologists [Samuels *et al.* 2010]. The ACR first started to hold two standalone training conferences in 2010 [Kaeley, 2010].

Developments in standardization

As ultrasound started to increase in popularity, it became apparent that there was a lack of standardization for the use of ultrasound in rheumatology. Consequently, in 2001, the first guidelines for musculoskeletal ultrasound in rheumatology were published by the EULAR Working Group for

Musculoskeletal Ultrasound [Backhaus *et al.* 2001]. However, there remained a lack of consensus regarding standardized ultrasound definitions of pathology as well as scanning methodology. This prompted a group of interested international rheumatology ultrasonographers to form Outcome Measures in Rheumatology (OMERACT), an ultrasound task force. This group developed the first consensus set of definitions for ultrasound pathologies based on the OMERACT filter [Boers *et al.* 1998] in the inflammatory joint diseases in 2005 [Wakefield *et al.* 2005], which has provided an initial framework for subsequent studies. This task force has been working towards the development of a standardized ultrasound scoring system for synovitis and an ultrasound joint count according to the OMERACT filter [D'Agostino *et al.* 2009]. Currently, this group is moving towards spondyloarthropathies, osteoarthritis, pediatrics and crystal arthropathies.

Advances in rheumatologic diseases and their assessment

Rheumatoid arthritis

Rheumatoid arthritis has been focused primarily in rheumatology ultrasound in terms of early detection, grading and treatment of synovitis. Since the first greyscale ultrasound demonstration synovitis of the knee joint, many studies have confirmed the superiority of ultrasound over clinical examination in the detection of synovitis, synovial hypertrophy, effusion and related pathologies [Grassi *et al.* 1993; Kane *et al.* 2003; Backhaus, 2009]. This is largely due to the fact that ultrasound can visualize minimally thickened synovium which is not yet perceivable by clinical palpation [Grassi, 2003; Kane *et al.* 2003; Karim *et al.* 2004]. Naturally, the next focus moved to how to assess synovitis using power or colour Doppler.

Doppler ultrasound is a technique that has been used widely in other medical ultrasonography areas such as cardiology, obstetrics and gastroenterology to evaluate blood flow of vessels. In rheumatology, especially in arthritis evaluation, the power Doppler technique is unique in terms of measurement of blood flow at a level of microvasculature (Figure 1). Power Doppler has been preferred to colour Doppler for the assessment of disease activity due to its technical advantages, including lack of aliasing, less angle dependency and greater sensitivity for low velocity blood flow. Thus, interest in whether power Doppler

Figure 1. Greyscale ultrasound can be used to demonstrate synovitis. In this image of a metacarpophalangeal joint of a patient with rheumatoid arthritis, the joint capsule is markedly distended outwards (arrows) due to underlying synovial effusion and hypertrophy. The presence of power Doppler demonstrates the increased microvascular flow of the joint, which is suggestive of active inflammation. M, metacarpal bone; P, proximal phalanx.

ultrasound is able to represent real inflammation within joints started in the early 2000s. Initial work has shown good correlation between Doppler hyperemia and histologically detected pannus [Schmidt *et al.* 2000] and rate of early synovial enhancement in magnetic resonance imaging (MRI) [Szkudlarek *et al.* 2001]. These results have been supported by other investigators who evaluated the relationship between Doppler hyperemia and histopathologic vascularity or MRI later on, confirming good correlation [Szkudlarek *et al.* 2001; Walther *et al.* 2001, 2002; Terslev *et al.* 2003b; Wiell *et al.* 2007; Bruyn *et al.* 2009, 2010].

With new definitions of primary pathologies, scoring systems were the next to be developed for both greyscale and colour Doppler. Different systems for both greyscale synovial hypertrophy and Doppler hyperemia have been proposed by different groups [Stone *et al.* 2001; Szkudlarek *et al.* 2003b]. The majority of these are semiquantitative using a 0–3 scale of mild, moderate and severe [Szkudlarek *et al.* 2003a]. These semiquantitative scorings are relatively easy to apply in clinical practice but the amount of difference between grades is not equal. Alternatively, scoring region of interest with continuous variables to quantify the degree of inflammation has been suggested. With Doppler in particular, more quantitative measures have been tested, such as the calculation of the resistive index or pixel counting in the region of interest [Terslev *et al.* 2003a, 2008; Fukae *et al.* 2010]. The downside of these measures, however, is their feasibility and they are probably only applicable to clinical trials.

A number of studies have started to investigate the role of ultrasound in patients with inflammatory arthritis with particular focus on bone erosion in

Figure 2. Transverse view through a second metacarpal head of a patient with rheumatoid arthritis. A well defined erosion can be seen which was confirmed in a longitudinal plane. M, metacarpal bone.

rheumatoid arthritis. An example of this is a study by Wakefield, which reported the superior sensitivity of ultrasound over radiography for the detection of bone erosions (Figure 2) in patients with rheumatoid arthritis [Wakefield *et al.* 2000]. In this study ultrasound detected 6.5- and 3.4-fold more erosions in 7.5- and 2.7-fold more patients than radiography in patients with early and late rheumatoid arthritis respectively. Following this study, several other reports have confirmed that ultrasound erosions show good concordance with MRI and computed tomography (CT) [Lopez-Ben *et al.* 2004; Dohn *et al.* 2006]. Although the OMERACT ultrasound group established an ultrasound definition of bone erosion, it does not include a size limit. As machine resolution continues to improve, distinguishing between small erosions and physiological bone abnormalities becomes even more important [Finzel *et al.* 2011]. Moreover, although scoring systems based on size [Wakefield *et al.*

2000] and semiquantitative scores [Reynolds *et al.* 2009] have been suggested, no consensus has been made on a standardized scoring system.

A relatively new area of discussion in rheumatoid arthritis has been which joints to assess by ultrasound in clinical practice and this has led to the concept of an ultrasound joint count. The ACR 66/68 clinical joint count for swelling and tenderness and the reduced 28-joint count have been widely used in rheumatology daily practice and clinical trials. However, these measures are not without limitations. Whether ultrasound can offer a more accurate and comprehensive method of evaluating joint inflammation and a more sensitive method of assessing response to therapies has been questioned. Thus, investigators have started to assess the value of assessing a number of different joint combinations. In 2005, the first ultrasound 28-joint count and index for effusion, synovitis and power Doppler signal showed good correlation with clinical variables [Naredo *et al.* 2005]. Subsequently, other ultrasound joint scoring systems using a 12-joint [Naredo *et al.* 2008], 7-joint [Backhaus *et al.* 2009], 44-joint [Scire *et al.* 2009], 38-joint [Filer *et al.* 2011] and 78-joint score [Hammer and Kvien, 2011] have been proposed and all demonstrated sensitivity to change. They differ from each other in terms of joints, tendons and bursae included. Acknowledging the need to reach agreement between the different scoring systems, the OMERACT/EULAR group has been working towards a common consensus on scoring systems for synovitis which are currently being tested in longitudinal studies. Ultimately however, the added value of using ultrasound in standard clinical care needs to be determined.

Until recently, compared with rheumatoid arthritis, less attention has been directed towards the role of ultrasound in the assessment and evaluation of other types of arthritis, including spondyloarthropathies, crystal-associated arthritis and osteoarthritis.

Spondyloarthropathies

The main use of ultrasound in spondyloarthropathies has been for the detection of enthesitis of the Achilles tendon and plantar fascia. In the first large study of 164 patients with spondyloarthropathy and 64 controls, a high prevalence of peripheral enthesal involvement was revealed by greyscale ultrasound combined with power

Doppler in patients with spondyloarthropathy. In this study, ultrasound clearly demonstrated its ability to be used to assess spondyloarthropathy activity [D'Agostino *et al.* 2003]. Other studies have focused on the ability of ultrasound to differentiate between subtypes of spondyloarthropathy [D'Agostino *et al.* 2003] and to distinguish spondyloarthropathies from rheumatoid arthritis [Falsetti *et al.* 2003]. As ultrasound demonstrated its usefulness in the evaluation of enthesial pathology, attempts have also been made to quantify enthesial abnormalities with ultrasound using different scoring systems such as the Sonographic Enthesitis Index [Alcalde *et al.* 2007] and the Madrid Sonographic Enthesis Index [De Miguel *et al.* 2009]. However, well reported methodology is lacking and consensus on elementary lesions and standardization of ultrasound examination is needed for future application in the evaluation of enthesitis [Gandjbakhch *et al.* 2011].

Osteoarthritis

The first ultrasonographic report on cartilage evaluation in rheumatology was published in 1992, in which a decrease of cartilage thickness in patients with osteoarthritis was reported. Ultrasound for osteoarthritis has gained less attention compared with rheumatoid arthritis, particularly because there are fewer treatment options for osteoarthritis. Recently the role of ultrasound to assess articular hyaline cartilage in osteoarthritis research has increased. Early and late changes of osteoarthritic cartilage, including loss of transparency and sharpness, which cannot be determined using conventional radiography, and decrease in thickness have been demonstrated since the mid 2000s [Borman *et al.* 2006; Meenagh *et al.* 2007; Filippucci *et al.* 2009; Kunkel, 2010; De Miguel *et al.* 2011; Ruta *et al.* 2011]. Moreover, a study reported that reduced cartilage shown by ultrasound may differentiate between early symptomatic osteoarthritis and early rheumatoid arthritis, suggesting measuring joint cartilage by ultrasound may be a promising alternative to conventional imaging [Moller *et al.* 2009]. In osteoarthritic joints, evidence suggests that synovitis is likely to occur, similar to rheumatoid arthritis, with an episodic aggravation that contributes to cartilage deterioration [Attur *et al.* 2010]. The use of ultrasound has allowed inflammatory changes to be examined, leading to new research about whether synovitis determined using ultrasound may play an active role in perpetuation of the disease. In the first attempt to

examine the relationship between ultrasound detectable changes and symptoms in hand osteoarthritis, painful joints were more likely to have ultrasound-detected greyscale and power Doppler synovitis [Keen *et al.* 2008]. Furthermore, a recent study demonstrated that joints with power Doppler signal had higher radiographic scores and lower cartilage thickness [Mancarella *et al.* 2010].

Crystal arthropathies: gout and pseudogout

Ultrasound studies began focusing on gout and pseudogout in the mid 2000s and showed different crystal deposit patterns within cartilage [Grassi *et al.* 2006; Thiele and Schlesinger, 2007]. At present, demonstrating the presence of monosodium urate (MSU) and calcium pyrophosphate dehydrate (CPPD) crystals in aspirated joint fluid or tophus is considered the gold standard for diagnosis [McCarty and Hollander, 1961]. However, this may change with the pictorial ability of high-resolution ultrasound. MSU and CPPD crystals can be detected with ultrasound when a conventional radiograph is normal [Frediani *et al.* 2005]. Once MSU or CPPD crystals are deposited in the articular cartilage, the sparkling nature of the deposited crystals makes them easier to be visualized, even for very small aggregates. The existence of a hyperechoic band over the anechoic hyaline cartilage surface, described as a double contour sign in gout, is a differentiating feature of the intracartilage deposit pattern of CPPD crystals and shows good sensitivity for the diagnosis of gout and CPPD disease [Grassi *et al.* 2006; Thiele and Schlesinger, 2007, 2010; De Miguel *et al.* 2011]. Currently, as a readily available tool, ultrasound may be helpful for the diagnosis of gout and pseudogout. More comprehensive data are needed to confirm its use for the early diagnosis and prevention of structural damage in patients with gout and pseudogout.

Vasculitis

The first major paper demonstrating the value of ultrasound in large vessel vasculitis was in 1995 [Schmidt *et al.* 1995]. This study reported a hypoechoic halo in temporal arteritis which disappeared 10–14 days after steroid treatment and suggested that ultrasound had the potential of replacing a temporal artery biopsy [Schmidt *et al.* 1997]. This work has subsequently been supported by another study [Nesher *et al.* 2002],

although large-scale multicenter studies have not been undertaken. To this end, larger-scale studies are underway to establish the true added value of ultrasound to the diagnosis of temporal arteritis and whether it can reliably replace the need for a biopsy. The scope of vasculitic ultrasound research has expanded to small vessels and other large-vessel arteritis. Vascular ultrasound has shown superiority over MRI and angiography in the visualization of carotid arterial wall affected by Wegener's granulomatosis [Schmidt *et al.* 2001] and is able to discriminate between different patterns of finger artery involvement in Wegener's granulomatosis, rheumatoid vasculitis and systemic sclerosis [Schmidt *et al.* 2006, 2008].

Salivary glands/Sjögren syndrome

Conventionally, minor salivary gland biopsy and sialography have been considered the cornerstones of the diagnosis of Sjögren syndrome. This concept has changed in the 2000s by an increasing number of studies assessing patients with Sjögren syndrome using ultrasound. Colour Doppler of patients with primary Sjögren syndrome has shown an increase in colour signal within the parenchyma and the resistive index or pulsatility index at the facial artery may reflect the vascular changes occurring in the salivary glands [Martinoli *et al.* 1994]. The structural changes, especially the parenchymal inhomogeneity demonstrated by ultrasound, were reported to have similar sensitivity to MRI [Makula *et al.* 2000]. In addition, the semiquantitative ultrasound score of the major salivary glands showed high diagnostic accuracy [Hocevar *et al.* 2005; Milic *et al.* 2009]. However, ultrasonographic classification criteria for primary Sjögren syndrome are still lacking and this has resulted in variable ultrasonographic diagnostic sensitivities of 43–93% and specificities of 64–100% for Sjögren syndrome [De Vita *et al.* 1992; Yonetsu *et al.* 2002; Milic *et al.* 2009]. Nevertheless, as ultrasound can visualize features of glandular involvement of primary Sjögren syndrome, it may replace invasive diagnostic procedures in patients suspected of having the syndrome [Salaffi *et al.* 2008].

Ultrasound-guided interventions

One of the major advantages with ultrasound is the improvements in the diagnostic and therapeutic musculoskeletal interventions in rheumatology clinical practice. By demonstrating structures

within and around joints, ultrasound has helped to increase the accuracy of injections. Although some studies could not demonstrate a better clinical outcome between blind and ultrasound-guided injection [Cunnington *et al.* 2010], real-time visualization of the needle tip and injected steroid crystals has made it possible to accurately inject steroids into the swollen tendon sheath, carpal tunnel and joint cavity, avoiding nearby neurovascular structures. Many studies have demonstrated the superiority of ultrasound-guided injection compared with blind injection guided by external anatomic landmarks in various synovial joints in terms of accuracy, safety and better clinical outcome [Koski, 2000; Sibbitt *et al.* 2009; Gilliland *et al.* 2011].

New research areas in the twenty-first century in rheumatology ultrasound

New developments in hardware and software technology have resulted in new applications, including contrast-enhanced ultrasound, three-dimensional (3D) and four-dimensional (4D) ultrasound, elastography and fusion imaging in rheumatology.

Contrast-enhanced ultrasound

The effect of microbubbles in increasing the backscattering of blood in Doppler ultrasound was first described in the aorta during cardiac catheterization [Gramiak and Shah, 1968]. This led to its application in many different disciplines, including liver, spleen and kidneys. Several types of microbubbles have been developed [Quaia, 2007]. In rheumatology, application of contrast-enhanced greyscale ultrasound began in the 2000s to maximize the spatial resolution using microbubbles. The use of 'first-generation' microbubble ultrasound contrast agent with power or colour Doppler resulted in improved detection of vascularity in the joints of patients with rheumatoid arthritis [Carotti *et al.* 2002; Klauser *et al.* 2002]. The new 'second-generation' ultrasound contrast agents have made microbubbles more stable and durable and therefore enabled continuous scanning to be performed over a specific period of time. Contrast-enhanced ultrasound has provided the differentiation of active synovitis from inactive intra-articular thickening, showing an ability to improve assessment of vascularized synovial proliferation in rheumatoid arthritis affected joints [Klauser *et al.* 2005]. The rate of uptake of

microbubbles can be measured by software packages produced by ultrasound manufacturers, which can provide quantitative data about the degree of vascularity. Furthermore, an exciting new potential role of microbubbles is the delivery of labelled microbubbles to specific anatomical sites either for further imaging studies or for the delivery of targeted drugs [Deshpande *et al.* 2011]. However, its use in rheumatology clinical practice has been limited by invasiveness, additional cost and time spent on the procedure, as well as the potential adverse reactions of microbubbles such as dyspnea, chest pain, hypotension or hypertension, nausea and vomiting. At present, quantification of contrast enhancement and standardization of measurements and interpretation need further investigation. However, the technique seems to have opened up new horizons in the sensitive assessment of synovitis, leading to evolution of contrast ultrasound from vascular imaging to imaging of perfused tissue at the microvascular level.

Three- and four-dimensional ultrasonography

The 3D technology and real-time update of the 3D volume, also known as 4D ultrasound, have been used mainly for fetal assessment and cardiology, but more recently they have been applied to rheumatology. The 3D ultrasound has been considered an interesting prospect for the assessment of musculoskeletal disease in terms of improving operator reliability. It has a unique advantage in that saved images can be viewed in coronal, and axial planes. The first 3D ultrasound study in rheumatology, reported in 2009, showed good to excellent agreement between two-dimensional (2D) and 3D ultrasound modalities relating to both joint inflammation and bone erosion [Filippucci *et al.* 2009]. Another report also demonstrated that interobserver reliability of 3D volumetric ultrasound in the detection of synovitis was higher than 2D ultrasound [Naredo *et al.* 2010]. One of the promising features of 3D ultrasound is its ability to quantify regions of interest (Figure 3), although no commercial software is available. The metric ability of 3D ultrasound can provide new advances in measuring lesions, but the metric quality according to the OMERACT filter should be established. It is likely that the use of 3D and 4D ultrasound will grow steadily in the future, but their application in musculoskeletal diseases has remained in the research domain in many rheumatology clinics [Ju *et al.* 2008].

Figure 3. Long axis two-dimensional ultrasound and corresponding three-dimensional (3D) ultrasound image of a small full thickness tear of the supraspinatus tendon. With appropriate multiplanar reconstruction, 3D ultrasound allows adequate delineation of the tear width and the amount of tendon retraction from the greater tuberosity (GT) [courtesy of Carlo Martinoli, MD and Paolo Nucci, PhD, Philips Healthcare].

Figure 4. Elastography of a degenerate Achilles tendon. The greyscale image shows relative preservation of the posterior tendon fibres but the mid and anterior portion is abnormal as evidenced by hypoechogenicity, loss of fibrillar pattern and thickening. Elastography represents tissue elasticity using a spectrum of colours – at one extreme, hard structures are denoted as blue and at the other, soft structures are seen as red. These images clearly show that elastography has the potential to differentiate between normal and abnormal portions of tendon. AT, Achilles tendon; Cal, calcaneum.

Elastography

The principle of strain imaging, which is known as elastography, was first reported in 1991 as a new ultrasound-based technique able to assess tissue elasticity [Ophir *et al.* 1991]. Later, a fast cross-sectional technique was developed, based on real-time elastography, which analyzes ultrasound echo signals while the probe compresses or relaxes the tissue [Pesavento *et al.* 1999]. In rheumatology, elastography was first used to evaluate changes in Achilles tendons in 2009 (Figure 4) [De Zordo *et al.* 2009a, 2009b]. Then, an elastography study of skin involvement in patients with systemic sclerosis showed the reduction of strain in the dermis of the forearm [Iagnocco *et al.*

2010]. Currently, additional data are needed on scleroderma and more validity and prospective studies are required to establish the true value of elastography.

Fusion imaging

The fusion imaging technique is the simultaneous mapping of ultrasound images onto a pre-acquired 3D multiplanar reslice CT or MRI volume dataset. The transducer needs adaptation to allow additional sensors to be positioned by means of a clip-on attachment. Fusion imaging may be useful for the differentiation of anatomical structures and injection of the sacroiliac joint

[Klauser *et al.* 2008]. In 2011, MRI/ultrasound real-time fusion imaging was first reported in patients with osteoarthritis and rheumatoid arthritis. Fusion imaging was able to provide consistent bony landmarks for potential longitudinal evaluation [Iagnocco *et al.* 2011]. However, its diagnostic and therapeutic role in rheumatic diseases has not yet been fully studied and requires further definition.

Conclusion

From the discovery of ultrasound to the application in rheumatology, musculoskeletal ultrasound has evolved in favour of early detection of joint inflammation, assessing ongoing disease activity and monitoring therapeutic responses. Consequently, musculoskeletal ultrasound is fast becoming an essential tool in routine clinical practice for rheumatologists. We anticipate that all rheumatology departments in the future will use ultrasound or have access to it. Similarly, it is likely that ultrasound techniques will start to be taught at an undergraduate level as it is fast becoming an integral part of other medical specialties as well. The technical advances expected in the future are likely to make musculoskeletal ultrasound more accessible to rheumatologists and allow faster and more accurate imaging of joints and related structures.

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Conflict of interest statement

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