A brief history of ultrasound in rheumatology: where we were

W. Grassi, E. Filippucci

Clinica Reumatologica, Scuola di Specializzazione in Reumatologia. Università Politecnica delle Marche, Ancona, Italy.

Walter Grassi, MD,
Emilio Filippucci, MD

Please address correspondence to:
Prof. Walter Grassi,
Clinica Reumatologica,
Scuola di Specializzazione in Reumatologia,
Università Politecnica delle Marche,
60035 Jesi (AN), Italy.
E-mail: walter.grassi@univpm.it

Received on December 4, 2013; accepted in revised form on December 10, 2013.

Clin Exp Rheumatol 2014; 32 (Suppl. 80): S3-S6.

Key words: ultrasound, rheumatology

Competing interests: none declared.

ABSTRACT

Ultrasonography in the '70s was a well-known and widely used method within several medical specialties but not in rheumatology. Initial development of the field was led by radiologists who mainly investigated the potential of ultrasound in the assessment of large joints.

In the late '80s, the first studies supporting the role of ultrasound in the detection of soft tissue changes and bone erosions in the hands of patients with rheumatoid arthritis were published.

In the '90s, the dramatic improvement of spatial resolution due to the new generation high frequency probes opened up new avenues for the exploration of otherwise undetectable anatomical details. Ultrasound research during this period was enhanced by the growing use of colour Doppler and power Doppler and by the first prototypes of three dimensional ultrasound. Over the last 10 years, the buzz words in ultrasound research in rheumatology have been standardisation, early diagnosis and therapy monitoring.

Once upon a time in Rheumatology land…

Many years ago all rheumatologists were blind. They were expert clinicians and excellent scientists capable of doing an infinity of things, but they could not look inside the body of their patients because of an ancient curse. Then, at the end of the last century something happened: some rheumatologists began to use a strange imaging tool that allowed them to look through the skin: it was an ultrasound machine. From that moment everything changed, but not quickly because rheumatologists were so accustomed to blindness that they did not feel any interest in this revolutionary new technique. Since ultrasound seemed to arouse interest especially among young rheumatologists it was defined as "a toy for the boy" and has largely been ignored by senior rheumatologists…. to be continued.

The 1970s

Ultrasonography in the 70s was a well known and widely used method within several medical specialties but not in rheumatology. Initial development of the field was led by radiologists. In 1972, ultrasound B-scanning was used in the differentiation of Baker's cyst and thrombophlebitis (1). In a short period of time ultrasound scanning was considered as the technique of choice for the detection and assessment of popliteal cysts (2). In 1978 Cooperberg *et al*. reported that grey-scale ultrasound at a frequency of 5.0 MHz was capable of detecting popliteal cysts, suprapatellar effusions and synovial thickening in the suprapatellar pouch of patients with rheumatoid arthritis (3). The time has not yet come to put forward additional applications of ultrasound in rheumatology.

The 1980s

In the early '80s, ultrasound was still mainly used for evaluating large joints and bursae. In 1981, Gompels and Darlington (4) successfully used ultrasound to facilitate the aspiration of synovial fluid for culture in a patient with septic arthritis of the shoulder. The authors also used ultrasound as a painless, non-invasive and safe method for the serial assessment of the joint after therapy. In 1982, ultrasound was used by Tiliakos *et al*. (5) to identify tophaceous *versus* rheumatoid nodules. In the same year, Fam *et al*. (6) demonstrated a high incidence of clinically unsuspected popliteal cysts in patients with symptomatic knee osteoarthritis. In 1984, Aisen *et al*. (7) opened up new horizons showing that ultrasound can be used to measure the thickness of the articular cartilage in humans, as well as to detect changes in its surface and internal characteristics. In 1986, Sattler and Schmidt (8) were probably the first rheumatologists to publish a comprehensive paper describing the potential of ultrasound in different rheumatic conditions affecting the elbow joint. In the same year, Baunin

et al. (9) demonstrated that ultrasound is a valuable tool in children with painful hip because of its ability to detect enlargement of joint cavity, effusion, synovial reaction and to allow a good survey. In 1987, Spiegel *et al*. (10) were the first to explore with a well-designed study the role of ultrasound in measuring disease activity in patients with rheumatoid arthritis.

The late '80s were characterised by several studies focused on the hip joint In 1989, Koski demonstrated the value of ultrasound in the diagnosis of hip synovitis in patients with rheumatoid arthritis (11). Over the following few years, Koski published several papers that strongly contributed to the progress of knowledge and to promote widespread interest in ultrasound. Koski can be regarded as the lone explorer of ultrasound in Rheumatology since he was the single author of most of his first papers. His research was mainly focused on large joints because the low frequency transducers that were available at that time did not allow a careful assessment of small joints (12, 13).

In 1988, the first description of ultrasound detection of bone erosion in rheumatoid arthritis was published by De Flaviis *et al*. (14). In 1990, Fornage (15) demonstrated the key role of ultrasound in detecting soft tissue changes in the hand of patients with rheumatoid arthritis, with specific reference to tendon involvement.

The 1990s

In the early '90s the main focus of ultrasound research was still on large joints (hip, knee, shoulder and elbow). In 1990, Kellner *et al*. (16) showed that ultrasound is able to detect calcifications both at the meniscal and wrist level in patients with chondrocalcinosis. In the same year, Koski (17), in a large group of patients, demonstrated that the measurement of the anechoic space between the bone and joint capsule of metatarsophalangeal joints and talocrural joints may be useful to differentiate healthy subjects from patients with arthritis. In 1992, Koski (18) also demonstrated that effusion in the hip and gleno-humeral joints are a common finding in patients with polymyalgia rheumatica.

An important step forward towards the enhancement of the ultrasound potential in rheumatology was the availability of the first prototypes of "small parts" probes with a frequency higher than 7.5 MHz.

The dramatic improvement of spatial resolution due to the new generation high frequency probes opened up new avenues for the exploration of otherwise undetectable anatomical details. Ultrasound quickly demonstrated its key role in the analysis of tendinous structure. In 1993, Martinoli *et al*. elegantly confirmed that the internal network of fine parallel and linear echoes that characterises tendinous echotexture is caused by specular reflections at the interface between collagen bundles and endotendineum septa (19). In the same year, the first study of the metacarpophalangeal joints in patients with rheumatoid arthritis with a 13 MHz probe was published by Grassi *et al*. (20). Ultrasound was able to detect a wide spectrum of abnormalities including joint cavity widening, effusion, synovial thickening, bone erosions, loss of definition of the metacarpal articular cartilage, widening of the flexor tendon sheath, irregularities of flexor and extensor tendons and tendon rupture.

The potential of ultrasound to provide morphological information of enthesis which is unobtainable by a clinical assessment of patients with spondyloarthropathy was clearly demonstrated by Lehtinen *et al*. in 1994 (21). The spectrum of sonographic changes included oedema at the insertion of the tendon, bursitis, focal intra-tendinous changes and periosteal changes. Ultrasound demonstrated its pivotal role in giving more detailed information about the causes of pain at the insertions of tendons.

From the mid '90s there was a dramatic increase of papers focused on the applications of ultrasound in several clinical conditions such as diagnosis of foot and ankle pathology, painful shoulder, acromio-clavicular joint pathology, differential diagnosis of juvenile hip pain, ileo-psoas bursitis, dactylitis, digital ganglia, psoriatic arthritis, seronegative spondyloarthritis, juvenile rheumatoid arthritis, polymyalgia rheumatic, osteoarthritis, crystal deposition diseases, hip arthritis, painful knee, septic arthritis, enthesitis, preoperative evaluation of tendons, intra-articular steroid injections, synovial biopsy, therapy monitoring

Ultrasound research during this period was enhanced by the growing use of colour Doppler and power Doppler and by the first prototypes of three dimensional (3D) ultrasound (22, 23). In 1999, Hau *et al*. (24) demonstrated that evaluation of pannus and the extent of vascularisation within the joints of patients with rheumatoid arthritis might be helpful in the assessment of disease activity in patients with rheumatoid arthritis. In 1994, Kellner *et al*. (23) reported the first results of 3D ultrasound in the assessment of large (hip), middle-sized (elbow) and small (finger, toe) joints.

Despite the growing evidence of the clinical value of ultrasound in daily clinical practice the dissemination of this imaging technique was surprisingly very limited over the '90s. In 1999, Donald Resnick wrote that "for some unexplained reason, ultrasonography applied to disorders of tendons, musculature, soft tissues, and even bones has been largely ignored by many physicians, particularly those in the United States" (25).

The third millennium

The early '2000s was still characterised by a constant increase of ultrasound studies. Wakefield *et al*. (26) demonstrated that ultrasound detects more erosions than conventional radiography, especially in early rheumatoid arthritis. Sonographically-guided procedures are clearly described and allow a relevant progress in the field of intralesional injection (27, 28). In 2001, Szkudlarek *et al*. showed that power Doppler ultrasound is a reliable technique for assessing inflammatory activity in the metacarpophalangeal joints of patients with rheumatoid arthritis, using dynamic MRI as the standard. In 2002, Hau *et al*. demonstrated that ultrasound was able to detect a decrease in pannus vascularisation of small finger joints in patients with rheumatoid arthritis one month after treatment with a tumour ne-

crosis factor alpha blocker (29). In the same year, Klauser *et al*. (30) reported that the use of a micro bubble-based ultrasound contrast agent significantly improves the detection of intra-articular vascularisation in the finger joints of patients with rheumatoid arthritis. Power Doppler ultrasound with an echo contrast agent has also proven to be a very useful tool in distinguishing between inflammatory and non-inflammatory pannus (31). In that year, Balint *et al*. demonstrated that ultrasound is better than clinical examination in the detection of entheseal abnormalities of the lower limbs in spondyloarthropathy (32) and that ultrasound greatly improves the rate of diagnostic synovial fluid aspiration, particularly in small joints (33). In 2003, Kane *et al*. (34) reported that ultrasound is more sensitive than clinical examination in the detection of suprapatellar bursitis, knee effusion, and Baker's cyst in rheumatoid arthritis. In the same year, Terslev *et al*. demonstrated that estimates of synovial inflammatory activity by Doppler ultrasound and post-contrast magnetic resonance were comparable (35).

Over the last 10 years, the buzz words in ultrasound research in rheumatology have been standardisation, early diagnosis and therapy monitoring (36, 37). A huge amount of work has been done by the members of the OMERACT task force for the development of widely accepted definitions and classifications (38-43). Ultrasound has also demonstrated its value in the management of crystal arthropathy (44, 45). The first comprehensive description of the wide spectrum of sonographic features due to urate and pyrophosphate crystal deposits was published in 2006 (46).

The constant progress in ultrasound technology has allowed amazing quality improvements of ultrasound images. Today, a high quality ultrasound apparatus is something like a Swiss knife with multiple capabilities including "acoustic microscopy options, high sensitivity power and colour Doppler, panoramic assessment of large anatomic areas, tomographic analysis, 3D reconstruction, elastosonography, and measurement of vessel wall stiffness. We can now clearly recognise anatomical details of less than 0.1 mm and detect even a minimal increase of blood perfusion in the target tissues of patients with very early arthritis. Thus, it is not surprising that ultrasound has revealed the potential to make a clinically relevant impact in the assessment of the extra-articular involvement of rheumatic diseases (salivary glands, skin, lung, and blood vessels) (47-53). However, even if the advent of ultrasound has led to a genuine revolution in the clinical decision making process there is every reason to think that the role of ultrasound is still in its infancy and will be even more relevant in the near future.

References

1. MCDONALD DG, GEORGE RL: Ultrasound B-scanning in the differentiation of Baker's cyst and thrombophlebitis. *Br J Radiol* 1972; 45: 729-32.
2. MOORE CP, SARTI DA, LOUIE JS: Ultrasonographic demonstration of popliteal cysts in rheumatoid arthritis. A noninvasive technique. *Arthritis Rheum* 1975; 18: 577-80.
3. COOPERBERG PL, TSANG I, TRUELOVE L, KNICKERBOCKER WJ: Gray scale ultrasound in the evaluation of rheumatoid arthritis of the knee. *Radiology* 1978; 126: 759-63.
4. GOMPELS BM, DARLINGTON LG: Septic arthritis in rheumatoid disease causing bilateral shoulder dislocation: diagnosis and treatment assisted by grey scale ultrasonography. *Ann Rheum Dis* 1981; 40: 609-11.
5. TILIAKOS N, MORALES AR, WILSON CH JR.: Use of ultrasound in identifying tophaceous versus rheumatoid nodules. *Arthritis Rheum* 1982; 25: 478-9.
6. FAM AG, WILSON SR, HOLMBERG S: Ultrasound evaluation of popliteal cysts on osteoarthritis of the knee. *J Rheumatol* 1982; 9: 428-34.
7. AISEN AM, MCCUNE WJ, MACGUIRE A *et al*.: Sonographic evaluation of the cartilage of the knee. *Radiology* 1984; 153: 781-4.
8. SATTLER H, SCHMIDT KL: Status of arthrosonography in rheumatologic diagnosis: examination technic, findings and their interpretation. I. The elbow joint. *Z Rheumatol* 1986; 45: 1-6.
9. BAUNIN C, MORENO P, CLÉMENT JL, RAILHAC JJ, CAHUZAC JP: Value of ultrasonics in painful hip in children. *Chir Pediatr* 1986; 27: 75-8.
10. SPIEGEL TM, KING W 3RD, WEINER SR, PAULUS HE: Measuring disease activity: comparison of joint tenderness, swelling, and ultrasonography in rheumatoid arthritis. *Arthritis Rheum* 1987; 30: 1283-8.
11. KOSKI JM: Ultrasonographic evidence of hip synovitis in patients with rheumatoid arthritis. *Scand J Rheumatol* 1989; 18: 127-31.
12. KOSKI JM: Axillar ultrasound of the glenohumeral joint. *J Rheumatol* 1989;16:664-7.
13. KOSKI JM, ISOMÄKI H: Ultrasonography may reveal synovitis in a clinically silent hip joint. *Clin Rheumatol* 1990; 9: 539-41.
14. DE FLAVIIS L, SCAGLIONE P, NESSI R, VENTURA R, CALORI G: Ultrasonography of the hand in rheumatoid arthritis. *Acta Radiol* 1988; 29: 457-60.
15. FORNAGE BD: Soft-tissue changes in the hand in rheumatoid arthritis: evaluation with US. *Radiology* 1989; 173: 735-7.
16. KELLNER H, ZOLLER W, HERZER P: Ultrasound findings in chondrocalcinosis. *Z Rheumatol* 1990; 49: 147-50.
17. KOSKI JM: Ultrasonography of the metatarsophalangeal and talocrural joints. *Clin Exp Rheumatol* 1990; 8: 347-51.
18. KOSKI JM: Ultrasonographic evidence of synovitis in axial joints in patients with polymyalgia rheumatica. *Br J Rheumatol* 1992; 31: 201-3.
19. MARTINOLI C, DERCHI LE, PASTORINO C, BERTOLOTTO M, SILVESTRI E: Analysis of echotexture of tendons with US. *Radiology* 1993; 186: 839-43.
20. GRASSI W, TITTARELLI E, PIRANI O, AVALTRONI D, CERVINI C: Ultrasound examination of metacarpophalangeal joints in rheumatoid arthritis. *Scand J Rheumatol* 1993; 22: 243-7.
21. LEHTINEN A, TAAVITSAINEN M, LEIRISALO-REPO M: Sonographic analysis of enthesopathy in the lower extremities of patients with spondyloarthropathy. *Clin Exp Rheumatol* 1994; 12: 143-8.
22. SILVESTRI E, MARTINOLI C, ONETTO F, NEUMAIER CE, CIMMINO MA, DERCHI LE: Evaluation of rheumatoid arthritis of the knee with Doppler color. *Radiol Med* 1994; 88: 364-7.
23. KELLNER H, LIESS H, ZOLLER WG: 3D-ultrasound of soft tissues and joints. *Bildgebung* 1994; 61: 130-4.
24. HAU M, SCHULTZ H, TONY HP *et al*.: Evaluation of pannus and vascularization of the metacarpophalangeal and proximal interphalangeal joints in rheumatoid arthritis by high-resolution ultrasound (multidimensional linear array). *Arthritis Rheum* 1999; 42: 2303-8.
25. CHHEM R, CARDINAL E: Guidelines and Gamuts in Musculoskeletal Ultrasound. Editor: Wiley-Liss (30 October 1998).
26. WAKEFIELD RJ, GIBBON WW, CONAGHAN PG *et al*.: The value of sonography in the detection of bone erosions in patients with rheumatoid arthritis: a comparison with conventional radiography. *Arthritis Rheum* 2000; 43: 2762-70.
27. GRASSI W, FARINA A, FILIPPUCCI E, CERVINI C: Sonographically guided procedures in rheumatology. *Semin Arthritis Rheum* 2001; 30: 347-53.
28. QVISTGAARD E, KRISTOFFERSEN H, TERSLEV L, DANNESKIOLD-SAMSÃ¸E B, TORP-PEDERSEN S, BLIDDAL H: Guidance by ultrasound of intra-articular injections in the knee and hip joints. *Osteoarthritis Cartilage* 2001; 9: 512-7.
29. SZKUDLAREK M, COURT-PAYEN M, STRANDBERG C, KLARLUND M, KLAUSEN T, OSTERGAARD M: Power Doppler ultrasonography for assessment of synovitis in the metacarpophalangeal joints of patients with rheumatoid arthritis: a comparison with dy-

namic magnetic resonance imaging. *Arthritis Rheum* 2001; 44: 2018-23.
30. KLAUSER A, FRAUSCHER F, SCHIRMER M *et al*.: The value of contrast-enhanced color Doppler ultrasound in the detection of vascularization of finger joints in patients with rheumatoid arthritis. *Arthritis Rheum* 2002; 46: 647-53.
31. CAROTTI M, SALAFFI F, MANGANELLI P, SALERA D, SIMONETTI B, GRASSI W: Power Doppler sonography in the assessment of synovial tissue of the knee joint in rheumatoid arthritis: a preliminary experience. *Ann Rheum Dis* 2002; 61: 877-82.
32. BALINT PV, KANE D, WILSON H, MCINNES IB, STURROCK RD: Ultrasonography of entheseal insertions in the lower limb in spondyloarthropathy. *Ann Rheum Dis* 2002; 61: 905-10.
33. BALINT PV, KANE D, HUNTER J, MCINNES IB, FIELD M, STURROCK RD: Ultrasound guided versus conventional joint and soft tissue fluid aspiration in rheumatology practice: a pilot study. *J Rheumatol* 2002; 29: 2209-13.
34. KANE D, BALINT PV, STURROCK RD: Ultrasonography is superior to clinical examination in the detection and localization of knee joint effusion in rheumatoid arthritis. *J Rheumatol* 2003; 30: 966-71.
35. TERSLEV L, TORP-PEDERSEN S, SAVNIK A *et al*.: Doppler ultrasound and magnetic resonance imaging of synovial inflammation of the hand in rheumatoid arthritis: a comparative study. *Arthritis Rheum* 2003; 48: 2434-41.
36. MURAYAMA G, OGASAWARA M, NEMOTO T *et al*.: Clinical miscount of involved joints denotes the need for ultrasound complementation in usual practice for patients with rheumatoid arthritis. *Clin Exp Rheumatol* 2013; 31: 506-14.
37. CHEUNG PP, GOSSEC L, RUYSSEN-WITRAND A, LE BOURLOUT C, MÉZIÈRES M, DOUGADOS M: The relationship of patient-reported joints with active synovitis detected by power Doppler ultrasonography in rheumatoid arthritis. *Clin Exp Rheumatol* 2013; 31: 490-7.
38. SCHMIDT WA, SCHMIDT H, SCHICKE B, GROMNICA-IHLE E: Standard reference values for musculoskeletal ultrasonography. *Ann Rheum Dis* 2004; 63: 988-94.
39. WAKEFIELD RJ, BALINT PV, SZKUDLAREK M *et al*.: Musculoskeletal ultrasound including definitions for ultrasonographic pathology. *J Rheumatol* 2005; 32: 2485-7.
40. WAKEFIELD RJ, D'AGOSTINO MA, IAGNOCCO A *et al*.: The OMERACT Ultrasound Group: status of current activities and research directions. *J Rheumatol* 2007; 34: 848-51.
41. D'AGOSTINO MA, CONAGHAN PG, NAREDO E *et al*.: The OMERACT ultrasound task force - Advances and priorities. *J Rheumatol* 2009; 36: 1829-32.
42. NAREDO E, WAKEFIELD RJ, IAGNOCCO A *et al*.: The OMERACT ultrasound task force – status and perspectives. *J Rheumatol* 2011; 38: 2063-7.
43. DOUGADOS M, JOUSSE-JOULIN S, MISTRETTA F *et al*.: Evaluation of several ultrasonography scoring systems for synovitis and comparison to clinical examination: results from a prospective multicentre study of rheumatoid arthritis. *Ann Rheum Dis* 2010; 69: 828-33.
44. FILIPPUCCI E, DELLE SEDIE A, RIENTE L *et al*.: Ultrasound imaging for the rheumatologist. XLVII. Ultrasound of the shoulder in patients with gout and calcium pyrophosphate deposition disease. *Clin Exp Rheumatol* 2013; 31: 659-64.
45. PEITEADO D, DE MIGUEL E, VILLALBA A, ORDÓÑEZ MC, CASTILLO C, MARTÍN-MOLA E: Value of a short four-joint ultrasound test for gout diagnosis: a pilot study. *Clin Exp Rheumatol* 2012; 30: 830-7.
46. GRASSI W, MEENAGH G, PASCUAL E, FILIPPUCCI E: "Crystal clear"-sonographic assessment of gout and calcium pyrophosphate deposition disease. *Semin Arthritis Rheum* 2006; 36: 197-202.
47. SALAFFI F, CAROTTI M, IAGNOCCO A *et al*.: Ultrasonography of salivary glands in primary Sjögren's syndrome: a comparison with contrast sialography and scintigraphy. *Rheumatology* 2008; 47: 1244-9.
48. GARGANI L, DOVERI M, D'ERRICO L *et al*.: Ultrasound lung comets in systemic sclerosis: a chest sonography hallmark of pulmonary interstitial fibrosis. *Rheumatology* 2009; 48: 1382-7.
49. DI GESO L, FILIPPUCCI E, GIROLIMETTI R *et al*.: Reliability of ultrasound measurements of dermal thickness at digits in systemic sclerosis: role of elastosonography. *Clin Exp Rheumatol* 2011; 29: 926-32.
50. KALOUDI O, BANDINELLI F, FILIPPUCCI E *et al*.: High frequency ultrasound measurement of digital dermal thickness in systemic sclerosis. *Ann Rheum Dis* 2010; 69: 1140-3.
51. SCHMIDT WA, KRAFT HE, VORPAHL K, VÖLKER L, GROMNICA-IHLE EJ: Color duplex ultrasonography in the diagnosis of temporal arteritis. *N Engl J Med* 1997; 337: 1336-42.
52. DI GESO L, ZARDI EM, AFELTRA A *et al*.: Comparison between conventional and automated software-guided ultrasound assessment of bilateral common carotids intima-media thickness in patients with rheumatic diseases. *Clin Rheumatol* 2012; 31: 881-4.
53. FILIPPUCCI E, MEENAGH G, EPIS O *et al*.: Ultrasound imaging for the rheumatologist. XIII. New trends. Three-dimensional ultrasonography. *Clin Exp Rheumatol* 2008; 26: 1-4.[0]