

EULAR Points to Consider for the use of imaging to guide interventional procedures in patients with Rheumatic and Musculoskeletal Diseases (RMDs)

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ABSTRACT

Objectives: To develop evidence-based Points to Consider (PtC) for the use of imaging modalities to guide interventional procedures in patients with rheumatic and musculoskeletal diseases (RMDs).

Methods: EULAR standardised operating procedures were followed. A systematic literature review was conducted to retrieve data on the role of imaging modalities including ultrasound, fluoroscopy, magnetic resonance imaging, computed tomography and fusion imaging to guide interventional procedures. Based on evidence and expert opinion, the task force (25 participants consisting of physicians, healthcare professionals and patients from 11 countries) developed PtC, with consensus obtained through voting. The final level of agreement was provided anonymously.

Results: A total of 3 overarching principles and 6 specific PtC were formulated. The task force recommends preference of imaging over palpation to guide targeted interventional procedures at peripheral joints, periarticular musculoskeletal structures, nerves and the spine. While ultrasound is the favoured imaging technique for peripheral joints and nerves, the choice of the imaging method for the spine and sacroiliac joints has to be individualized according to the target, procedure, expertise, availability and radiation exposure. All imaging guided interventions should be performed by a trained specialist using appropriate operational procedures, settings and assistance by technical personnel.

Conclusion: These are the first EULAR PtC to provide guidance on the role of imaging to guide interventional procedures in patients with RMDs.

Keywords: Arthritis, Rheumatoid; ultrasonography; magnetic resonance imaging; orthopaedic procedures.

KEY MESSAGES

What is already known about this subject?

1. Imaging is increasingly used to guide interventional procedures in patients with rheumatic and musculoskeletal diseases (RMDs)
2. Imaging guided procedures require additional preparation and training as compared to palpation guided interventions
3. Uncertainty persist amongst clinicians on which imaging technique should be used to optimally guide interventional procedures

What does this study add?

1. These are the first EULAR endorsed Points to Consider for the use of imaging to guide interventional procedures in patients with RMDs

How might this impact on clinical practice or future developments?

1. These Points to Consider give advice to clinicians in which clinical situation, for which intervention, and in which anatomical area imaging should be used to guide interventional procedures
2. The research agenda highlights the gaps in evidence and areas of future studies

INTRODUCTION

Interventional procedures such as fluid aspiration, injections and biopsies are conducted for diagnostic and therapeutic purposes in patients with different rheumatic and musculoskeletal diseases (RMDs).[1] Real-time visualization of the needle or instruments by ultrasound (US), computed tomography (CT), magnetic resonance imaging (MRI) or fluoroscopy has the potential to ensure reliable placement of the needle tip/instrument in the respective anatomical area and to monitor the success of various interventions such as synovial fluid aspiration, drug injection and/or tissue biopsy.[2–6] Imaging guided procedures, however, are also more resource consuming than conventional palpation guided interventions, require additional preparation and training, and there are some studies suggesting that the outcomes of palpation and imaging guided interventions are not meaningfully different.[7,8] Clinicians are therefore still uncertain in which clinical situation, for which intervention, and in which anatomical area imaging should be used to guide interventional procedures. Advice is also needed for the setting (e.g. sterility of the room, assistance by nurses) and procedural techniques (e.g. direct vs. indirect aspiration/injection technique).

The broad objective of this project is to provide European Alliance of Associations for Rheumatology (EULAR) endorsed, evidence-based Points to Consider (PtC) for the use of imaging to guide interventional procedures in patients with RMDs.

METHODS

After approval by the EULAR Council, the convenors (CDe and XB) and the methodologist (PMM) led a task force guided by the 2014 updated EULAR standardised operating procedures (SOPs).[9] The 25 task force members consisted of rheumatologists, radiologists [all were members of the European Society of Musculoskeletal Radiology (ESSR)], orthopaedic surgeons, patient representatives, methodologists, a healthcare professional, and two EMerging EUlar NETwork (EMEUNET) representatives from 11 countries. All members disclosed their potential conflicts of interest before the start of the process. A hygienist (which is a specialist committed to the prevention of intra-hospital infections, including the prevention of surgical site infections), external to the task force, was consulted to discuss and advise the task force regarding the proposals on preparations to conduct interventions with direct imaging guidance detailed in Box 1. One face-to-face and two virtual task force meetings took place, as well as interim e-mail based feedback on the draft PtC. The second meeting was originally scheduled as a face-to-face meeting, but was then transformed into a virtual event due to the restrictions imposed by the COVID-19 pandemic.[9] Since another face-to-face meeting was recommended by EULAR SOPs in order to discuss and vote on the final PtC, a 3rd meeting was scheduled but had ultimately to be transformed again into a webinar due to COVID-19.

At the first meeting (face-to-face), the task force agreed on three broad research questions: 1) What is the value of imaging methods (US, CT, MRI, fluoroscopy/x-ray, fusion imaging) to guide interventional procedures in patients with RMDs, 2) what is the value of different imaging settings and technical standards, and 3) what is the value of different procedural techniques for imaging guided interventions.

A single systematic literature review (SLR) was conducted by two fellows (PB and FC) under the guidance of the methodologist (PMM). The convenors, together with the methodologist and fellows translated the research questions in the PICO (Population, Intervention, Comparator, Outcome) format (see supplementary Table 1 and [10]). The search strings were developed by an experienced librarian (LF) and applied to MEDLINE, EMBASE, the Cochrane Library and Epistemonikos databases (through 10/21). Prospective and retrospective full research articles, short reports and letters including original (patient) data, published in English and comparing different (imaging) techniques, different settings and procedural protocols to guide interventions in patients with RMDs were retrieved. Risk of bias (RoB) was assessed using the Cochrane RoB tool for randomized trials version 2 (ROB2), the RoB tool for non-randomized studies of Interventions (ROBINS-I) and the appraisal tool for cross-sectional studies (AXIS).[11–13] The evidence summarized in the SLR was presented during the second and third task force meetings. Data were summarized in the form of tables including the risk of bias assessment. The SLR is published separately; however, it forms an integral and inseparable part of the present PtC manuscript and should be read as such.

At the second meeting (virtual), the task force formulated the PtC based on the evidence and expert opinion in a process of discussion and consensus. Subsequently,

the draft PtC underwent structured written feedback from the task force members. At the third meeting (virtual), the PtC were refined based on the updated evidence (i.e. articles published between 2nd and 3rd task force meeting) and feedback received, followed by voting on the PtC. Consensus was accepted if >75% of the members voted in favour of the PtC at the first round, ≥67% at the second round and at a third round >50% was accepted.[14] The Oxford centre for evidence based medicine 2011 levels of evidence (LoE) derived from the SLR were added to each PtC.[15]

Subsequently, each task force member anonymously indicated the level of agreement via Survey Monkey® (LoA, 0-10 numeric rating scale ranging from 0= "completely disagree" to 10= "completely agree"). The mean and standard deviation of the LoA, as well as the percentage of task force members with an agreement ≥8 are presented.

Based on the gaps in the evidence and controversial points, a research agenda was formulated. The manuscript was reviewed by the EULAR Council and a revised version was finally approved by all task force members and the EULAR Council.

RESULTS

General aspects

These PtC are intended to advise qualified (physician and non-physician) healthcare professionals including rheumatologists, paediatricians, orthopaedic surgeons, neurosurgeons, radiologists, specialists in physical medicine and rehabilitation or sports medicine, general practitioners, anaesthesiologists and physical therapists on the use of imaging modalities to guide interventional procedures in patients with RMDs. These PtC are not intended to cover all aspects of interventional procedures; we explicitly excluded interventions with the purpose of local or regional anaesthesia before surgery, interventions concerning tumours, vessels or glands as well as arthroplasty and vertebroplasty.

The task force defined “targeted” interventions as procedures requiring a high level of precision to reach a specific anatomical area such as injection of small ganglia, cysts or tenosynovitis, aspiration of small amounts of fluid or synovial biopsy.

The population of interest is patients with RMDs (degenerative, inflammatory or autoimmune) including patients with painful joints, tendons, entheses and/or muscles, as well as neuropathic pain or discomfort.

These PtC may also inform patients participating in shared-decision making and healthcare provider organizations arranging care for RMD patients.

A total of 3 overarching principles and 6 specific PtC have been formulated. They are summarized in **Table 1** (including the LoE and LoA) and are discussed in detail below.

Table 1. EULAR Points to Consider (PtC) for the use of imaging to guide interventional procedures in patients with rheumatic and musculoskeletal diseases (RMD)

Overarching principles	LoE	LoA
A. The imaging technique should be optimized according to the procedure and the anatomical site taking into account potential side effects, radiation exposure, availability, expertise and costs.	n.a.	10.0 (0.2) 100% ≥ 8
B. Imaging guided interventional procedures should be conducted under adequate aseptic conditions (as detailed in Box 1).	n.a.	10.0 (0.2) 100% ≥ 8
C. Complex imaging guided interventional procedures should be conducted with adequate assistance by technical personnel.	n.a.	9.5 (1.7) 91.7% ≥ 8
Specific Points to Consider		
1. Imaging should be preferred over palpation to guide targeted* interventional procedures at peripheral joints and periarticular structures in patients with RMDs.	3 [#]	9.7 (0.5) 100% ≥ 8
2. Ultrasound should be used as the first imaging modality for interventional procedures at peripheral joints. Fluoroscopy may be used as an alternative.	3 [#]	9.1 (2.1) 95.8% ≥ 8
3. Imaging should be preferred over palpation to guide targeted* injections at structures encompassing peripheral nerves. Ultrasound should be the preferred imaging modality.	3 [#]	9.9 (0.3) 100% ≥ 8
4. Imaging should be used to guide targeted* injections at the spine.	5	9.9 (0.3) 100% ≥ 8
5. Imaging should be preferred over palpation for targeted* injections of the sacroiliac joint(s).	3 [#]	9.9 (0.3) 100% ≥ 8
6. Healthcare professionals performing imaging guided interventional procedures must have adequate skills in the respective imaging technique and the interventional procedure.	5	8.9 (2.9) 87.5% ≥ 8

LoA, level of agreement; LoE, Level of evidence; RMDs, rheumatic and musculoskeletal diseases, n.a., not applicable.

Numbers in column “LoA” indicate the mean and standard deviation (in parenthesis) of the LoA (range 0-10 with 0= “completely disagree” to 10= “completely agree”), as well as the percentage of task force members with an agreement ≥ 8 .

*Targeted interventions are defined as procedures requiring a high level of precision to reach a specific anatomical area such as injection of small ganglia, cysts or tenosynovitis, including aspiration of small amounts of fluid or synovial biopsy

#Levels of evidence were downgraded (from level 2 to level 3) because of bias related to randomisation, outcome assessment (trials and non-randomized studies), the population of interest (cross-sectional studies) and inadequate adjustment of potential confounders.

Overarching principles

These refer to principles of a generic nature. They are not necessarily based on specific levels of evidence but reflect issues of good clinical practice and the task force considered them as a framework for the subsequent, specific PtC.

A. The imaging technique should be optimized according to the procedure and the anatomical site taking into account potential side effects, radiation exposure, availability, expertise and costs.

The term “technique” refers not only to the choice of the imaging device, but also to the technical procedure such as direct visualisation of the needle during the intervention as compared to indirect imaging guidance where the exact position of the target is marked first using imaging followed by blind intervention, in or out of plane needle guidance etc., and the materials used such as different types of needles or other devices. Imaging may also support the decision of whether an intervention will be conducted by palpation or imaging guidance. A joint filled with synovial proliferation for example, might be markedly swollen but contain a small amount of fluid only. Aspiration guided by palpation might not be successful in such a situation, while imaging may help to reach the target easily. Another, less intuitive application of imaging is to confirm whether a target has been reached by an intervention guided by palpation. Evidence from the literature is absent for the majority of these aspects and the material/equipment available might differ between countries and hospitals/practices. High level of expertise for a given procedure was considered more relevant than developing a standard protocol for every possible situation, therefore, the task force made a specific PtC on skills and training below. In addition, radiation exposure should be balanced against expected accuracy and procedural safety of the intervention, and judgment may be different when the intervention is performed in young adults or children as compared to elderly people.

A related aspect is the relevance of in- versus out-of-target interventions. For some indications such as injection of trigger finger, clinical studies reported no difference for whether an injection was inside or outside flexor tendon sheaths in terms of safety and clinical efficacy.[16,17] In contrast, studies on joint interventions reported higher levels of pain in case glucocorticoid injections were extra- as compared to intra-articular.[18,19] For epidural injection of the spine or tissue biopsy, in-target placement of the needle is mandatory in order to avoid nerve damage or to obtain a representative biopsy sample, respectively. An overview of clinical studies retrieved by the SLR comparing different procedural protocols for imaging guided interventions is depicted in **Table 2**. Details of the studies cited are summarized in the SLR accompanying these PtC.[10]

Table 2. Overview of studies identified by the systematic literature review (SLR) investigating different procedural protocols for imaging guided interventions in RMD patients

Intervention	Comparator	Results for intervention
Intraarticular injections in sacroiliitis and ACJ arthritis[8,18,19]	Periarticular	Superior for short-, [19] and long-term pain[18]
Shoulder joint injections in adhesive capsulitis[20,21]	SASD bursa	Superior for short, [21] and long-term pain. [20,21] Mixed results for efficacy
Subscapularis muscle injection in scapular pain[22]	Scapulothoracic bursa	No difference in safety and efficacy
Medial access for knee injections in OA[23,24]	Midlateral- /Superolateral access	No difference in safety and accuracy
US in-plane injection in knee OA[25]	US out-of-plane	No difference in accuracy, adverse events, or procedural time
Bone biopsy in suspected osteomyelitis[26]	Paravertebral soft tissue	No difference in tissue acquisition
Intra-tendon sheath injection in trigger fingers [27,28]	Extra tendon sheath	No difference in safety and efficacy
Intra-epineurium injections in CTS [29]	Extra-epineurium	Superior for symptom severity and efficacy
Ulnar access for injection in CTS[30,31]	Midline/radial access	Inferior for long-term pain reduction compared to radial access[30]
Injection above the median nerve in CTS[32]	Injection under the median nerve	No difference in safety and efficacy

ACJ; Acromioclavicular joint; CTS, carpal tunnel syndrome; OA, osteoarthritis; SASD, subacromial/subdeltoid; US, Ultrasound.

B. Imaging guided interventional procedures should be conducted under adequate aseptic conditions.

While every procedure penetrating the skin of a patient must be aseptic, the level of sterility may vary. The type of intervention (e.g. injection versus biopsy or direct versus indirect imaging guidance), the anatomical site (e.g. entheses versus spine) and the immunocompetency of the patient are some of the factors that may influence how “aseptic” the setting should be.

Studies comparing different measures to guarantee the sterility of imaging guided interventional procedures are absent, and most of the studies retrieved by the SLR were relatively vague in the description of what preparations were made.[10] Based on expert opinion, and considering current clinical practice, the task force proposed preparations to conduct interventions with direct imaging guidance under aseptic conditions in relation to the presumed risk of infection (**Box 1**). Preparation of procedures with indirect imaging guidance (i.e. conduction of imaging first followed by a blind intervention) are identical to palpation guided interventions described elsewhere.[1] The suggestions in Box 1 are not intended to cover every clinical situation nor to reflect all national guidelines. Some authorities for example, recommend using sterile gel for ultrasound guided interventions which is not current practice in every EULAR country [33,34]. In a severely immunocompromised patient undergoing highly invasive interventions (e.g. tissue biopsy at the spine) even more intensive preparations than those listed in Box 1 (such as using an operation theatre, surgical aseptic hand washing and wearing surgical gowns) may be required to minimize the risk of infection. Likewise, face masks are obligatory during the COVID-19 pandemic in many countries for patients, physicians and healthcare professionals along with a negative SARS-CoV2 test for patients, however, it is not clear, whether face masks reduce the risk of infection in simple imaging guided interventions such as joint injections, once the pandemic is over.

Box 1. Preparations to conduct interventions with direct imaging guidance in situations of low (L) and high risk of infection (H)

- Disinfection of the hands (L) or handwashing and disinfection (H)
- Gloves (L), alternatively sterile gloves (H)
- Sterile preparation of equipment (L,H)
- Disinfection of the injection site (L,H)
- For US guided interventions
 - maintenance of at least 0.5 cm between the probe/gel# and the needle (L) or
 - extensive disinfection of the probe and use of antiseptic instead of gel (L)
 - sterile vinyl foil cover for the US probe and sterile gel (H)
- Face masks* and cap (H)
- Sterilized wraps with opening to expose the applicable site only (H)

#use of sterile gel for ultrasound guided interventions is recommended by some national authorities

*obligatory for patients and healthcare provider in several countries during the COVID-19 pandemic

L, low risk of infection; H, high risk of infection

C. *Complex imaging guided interventional procedures should be conducted with adequate assistance by technical personnel.*

The task force agreed that complex imaging guided procedures such as synovial tissue biopsies should be supported by technical personnel. Simple interventions such as US guided intra-articular injections could, at least in theory, be managed without assistance even though the experts were of the opinion that every imaging guided intervention benefit from assistance, particularly to maintain sterility of the setting and to ensure a high accuracy of the procedure. Technical personnel are also required to prepare equipment and drugs, to assist the procedure and to help monitoring of patients' clinical status during and after the procedure, when needed. Literature is scarce about the possible benefit of technical assistance for the prevention of adverse events as well as for cost-effectiveness; these issues should be clarified by future studies.

Specific Points to Consider

Point to Consider 1: Imaging should be preferred over palpation to guide targeted interventional procedures at peripheral joints and periarticular structures in patients with RMDs.

The task force recognized that not all interventions at peripheral joints and periarticular structures (which include tendons, ligaments, entheses, pulleys and bursae) require imaging guidance, that imaging is not available in every setting and/or that professionals conducting interventions may not have sufficient expertise with imaging guidance. Synovial fluid aspiration of an extensively swollen knee, non-targeted injection of a metacarpophalangeal joint in a patient with rheumatoid arthritis, injection of the subacromial bursae in a patient with rotator cuff disease, injection of a trigger finger or enthesitis at lateral epicondyle might well be guided by palpation. In contrast, targeted interventions should be conducted under imaging guidance in order to guarantee a high accuracy of the procedure. The absence of immediate access to imaging, however, should not delay an urgent diagnostic procedure such as arthrocentesis in case of suspected septic arthritis.

Evidence from clinical studies indicate a better accuracy (including correct needle placement and superiority in tissue and fluid acquisition) and safety (less procedural and post-procedural pain and discomfort) for imaging than for palpation guided interventions whereas data regarding short- and long-term efficacy are contrasting.[10] The most important limitation of these studies, however, is that they did not detangle easy (e.g. subcapsular space of a highly swollen joint) from difficult to reach targets (e.g. small ganglion compressing a peripheral nerve). Accordingly, the task force had to extrapolate the evidence to conclude that imaging should be preferred when a high level of precision is needed in order to reach a specific anatomical area.

Studies on costs of imaging guided interventions at peripheral joints are available only for the USA reporting large differences of costs depending on the setting and reimbursement policies of individual insurance companies.[35–37] Whether imaging guided interventions are cost-effective in the USA and EULAR countries (e.g. by preventing secondary direct and indirect costs due to higher efficacy and/or lower rate of complications) is unclear so far. This aspect has been added to the research agenda.

Point to Consider 2: *Ultrasound should be used as the first imaging modality for interventional procedures at peripheral joints. Fluoroscopy may be used as an alternative.*

The majority of studies at peripheral joints were available for US and fluoroscopy with comparable results concerning efficacy and accuracy.[10] While fluoroscopy is still widely used in clinical practice,[38] the task force agreed that US should be preferred over fluoroscopy if both techniques were available with similar expertise, because of the absence of radiation, the better visualisation of soft tissue and the lower resource consumption by the former, as well as the fact that US can be used as part of everyday

clinical practice.[37,39] The European Union directive 2013/59/EURATOM states that if a non-radiating imaging modality is available, it should be invariably used and preferred over a modality which uses ionizing radiations.[40] Fluoroscopy is a valid alternative, particularly if US is not available, for joint aspiration and intra-articular injections.[41]

Other imaging modalities to guide interventional procedures of peripheral joints such as CT, MRI or fusion imaging are still a matter of research.

Point to Consider 3: *Imaging should be preferred over palpation to guide targeted injections at structures encompassing peripheral nerves. Ultrasound should be the preferred imaging modality.*

The task force emphasized that imaging is particularly helpful when a specific target, for example a cyst or ganglion compressing a peripheral nerve, should be injected. One study reported a higher efficacy of intra- than extra-epineural injection of the median nerve in patients with carpal tunnel syndrome for symptom improvement as well as for reduction of nerve swelling.[29] It is almost impossible to safely reach such a small anatomical place without imaging, even though a comparison between imaging and palpation guidance for this intervention is still missing.

The highest number of studies, most of them with low quality, were available for the comparison between US and palpation guided injections at the carpal tunnel.[10] Some of them reported more adverse events in patients undergoing palpation guided injections (e.g. hand weakness, finger numbness, skin discoloration or subcutaneous fat atrophy) [42,43] whereas others found no difference in terms of safety and efficacy. [10] The task force members recognized that most studies might have been underpowered to detect rare adverse events such as accidental nerve puncture or injury of the persistent median artery, particularly in patients with anatomical variants of the median nerve. Based on clinical experience, such adverse events can easily be avoided if imaging is used to guide the injections. A bifid median nerve is the most common anatomical variant occurring in 15-20% of the population, 11% have a persistent median artery.[44,45]

Evidence on imaging guided injections at peripheral nerves outside the carpal tunnel is scarce and mainly derives from observational and cadaveric studies,[46–51] hence this aspect has been included in the research agenda.

Fluoroscopy is not recommended for this indication because of the absence of data from trials and the fact that nerves cannot be visualised directly with this technique. The value of other imaging methods such as MRI, or CT with/without fusion with US to guide interventions at peripheral nerves still needs to be elucidated.

Point to Consider 4: *Imaging should be used to guide targeted injections at the spine.*

It is common clinical practice to use imaging for injections at the spine as demonstrated by a recent survey and according to experience of the task force members.[38] In clinical practice, the choice of the technique depends on the target (US or fluoroscopy

may be adequate for injections at facet joints whereas peri-radicular and epidural injections are mostly guided by CT), disease stage (CT or fusion imaging between CT/US or MRI/US may be used in cases with advanced degenerative disease or other structural damage at the spine),[52,53] local expertise and availability. Clinical studies comparing different techniques are virtually absent; a single study compared fluoroscopy with CT to conduct biopsies in case of suspected vertebral osteomyelitis revealing a better performance of the former, given its ability to adjust the needle in a vertical plane.[54] Facet joint injections are sometimes conducted under clinical guidance,[38] the percentage of in-target administration of the drug, safety and efficacy of this approach as compared to imaging guidance, however, is probably low (even though direct evidence is missing). MRI is rarely used to guide injections at the spine and there are little data from clinical studies to support its use.[10]

Point to Consider 5: *Imaging should be preferred over palpation for targeted injections of the sacroiliac joint(s).*

While injections of the sacroiliac joints are sometimes guided by palpation in clinical practice, the probability to reach the joint space is less than 25%.[55] Using imaging to guide injections and other interventions such as synovial tissue biopsy increases the accuracy of the procedure dramatically. One study reported that the joint space was reached in 85% of cases if US guidance was used,[56] and others found in-target needle placement in 91% of fluoroscopy guided injections.[41] Most efficacy and safety outcomes, however, were similar, independent of whether the injection was intra- or periarticular.[8,18] The follow-up time as well as the power of these studies to detect clinical differences, however, were limited and might thus have underestimated the true benefit of releasing drugs in- rather than outside the joint capsule.

The choice of the most appropriate imaging modality such as US, fluoroscopy, CT and MRI for sacroiliac joint injections is determined by local expertise and availability as well as by considerations of radiation exposure. Fusion imaging between US and CT might be helpful in case bony spurs or other type of joint damage limit the anatomical passage into the joint space.[57]

Point to Consider 6: *Healthcare professionals performing imaging guided interventional procedures must have adequate skills in the respective imaging technique and the interventional procedure.*

According to local rules and legal framework, non-physician healthcare professionals may also conduct imaging guided interventions, however, the task force strongly endorses specific training of all professionals performing these procedures. The amount of training depends on the technique and on local training requirements. EULAR has defined competencies in musculoskeletal US, and US guided interventions are part of intermediate and advanced level EULAR US courses, however, the task force considered it beyond the scope of this project to define the specific skills qualifying for imaging guided interventional procedures. Evidence from clinical studies is missing, hence this item has been added to the research agenda.

Based on the discussions and the areas of uncertainty, a research agenda has been proposed, depicted in **Box 2**.

Box 2. Future research agenda

- To compare the efficacy and accuracy of interventions guided by US, fluoroscopy, CT, MRI or fusion imaging at peripheral joints, nerves and the spine and for different indications (e.g. injections, arthrocentesis or biopsy; inflammatory versus non-inflammatory conditions).
- To compare imaging versus palpation guided interventions at different anatomical sites.
- To compare the safety and accuracy of imaging guided interventions conducted with and without technical personnel assisting the procedure.
- To develop and use outcome measures with importance to society including assessment of sick-leave days, cost-effectiveness and health resource consumption in studies on interventional procedures.
- To identify and agree upon outcomes measuring the success of interventional procedures (e.g. amount of fluid aspiration, quality of the samples in case of biopsies, long-term pain reduction in case of injections)
- To study the value of MRI, CT and/or fusion imaging for interventions at peripheral nerves, to study the value of US for interventions at nerves outside the carpal tunnel.
- To study the value of imaging to avoid accidental nerve trauma as compared to palpation guided injections.
- To investigate the effect of specific training programs on the accuracy of imaging guided interventional procedures and to assess the learning curve of professionals conducting imaging guided interventions.
- To define standard procedural protocols for imaging guided interventions.
- To investigate the effect of different levels of aseptic conditions on the prevalence of infections in imaging guided interventions.
- To evaluate the effect of echo-tip needles and needle visualization US software for the accuracy of imaging guided interventions.
- To compare different techniques and equipment for imaging guided interventions at different anatomical sites.

CT, computerized tomography; MRI, magnetic resonance imaging; US, ultrasound

DISCUSSION

These are the first EULAR PtC providing up-to-date guidance for the role of imaging to guide interventional procedures in patients with RMDs.

These principles are reflected in both the PtC and the research agenda, acknowledging also the gaps in evidence that include direct comparisons between different imaging modalities as well as the low amount of data on imaging guided interventions at peripheral nerves (particularly outside the carpal tunnel) and the spine. Besides, outcomes to measure the success of interventions (e.g. amount of fluid or quality of samples in case of arthrocentesis or biopsy, respectively, reduction of damage to surrounding structures, long-term pain reduction by injections), are elusive and should be defined by future research.

Where evidence from clinical trials was controversial or absent, PtC were formulated on the basis of current clinical practice and expert opinion.[38] Good quality studies are now required to answer the numerous questions raised in the research agenda, so that future PtC can be upgraded and based on more solid evidence. The present PtC nevertheless represent a step forward in the approach to conduct interventional procedures using imaging, complementing recent EULAR recommendations for intra-articular therapies.[1] We believe that their implementation will improve patient care.

A concern is publication bias assuming that negative studies or studies demonstrating that palpation guided interventions are superior over imaging guidance were probably less frequently published. Another limitation is that the task force was mainly composed of specialists using imaging regularly, even though they also conduct palpation guided interventions routinely. Expert opinion might nevertheless be biased towards a preference of imaging over clinical guidance of interventions.

In summary, we developed 3 overarching principles and 6 specific PtC on the use of imaging for interventional procedures in RMD. These PtC are supported by evidence along with expert consensus. Unresolved issues and areas of further study have been depicted in the research agenda. We expect that much progress continues taking place in the area of imaging in RMDs, and we will carefully follow developments in the field, assuming that an amendment of these PtC may be needed within a few years.

COMPETING INTERESTS

CD has received consulting/speaker's fees from Abbvie, Eli Lilly, Janssen, Novartis, Pfizer, Roche, Galapagos and Sanofi, all unrelated to this manuscript

PMM has received consulting/speaker's fees from Abbvie, BMS, Celgene, Eli Lilly, Galapagos, Janssen, MSD, Novartis, Orphazyme, Pfizer, Roche and UCB, all unrelated to this manuscript, and is supported by the National Institute for Health Research (NIHR), University College London Hospitals (UCLH), Biomedical Research Centre (BRC).

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HBH has received fees for speaking and/or consulting from AbbVie, BMS, Pfizer, UCB, Roche, MSD and Novartis.

WH has received fees for speaking and/or consulting from AbbVie, Alpinion, Canon, Celgene, Chugai, Janssen-Cilag, Pfizer, Roche.

CDu has received consulting/speaker's fees from Abbvie, BMS, Eli Lilly, Janssen, Novartis, Pfizer, Roche and UCB, all unrelated to this manuscript

PVB has received consulting/speaker's fees from Abbvie, BMS, Celgene, Celltrion, Eli Lilly, IBSA, Janssen-Cilag, MSD, Novartis, Pfizer, Professional Publishing Hungary, Richter, Roche, Sandoz, Springer Nature, UCB, all unrelated to this manuscript.

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CONTRIBUTORS

All authors were involved in the discussion and formulation of the Points to Consider. CDe wrote the first version of the manuscript. All authors reviewed it and made extensive comments and appropriate changes to it. All authors approved the final version of the manuscript.

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ETHICAL APPROVAL INFORMATION

Not applicable, since no patients' data were acquired.

DATA SHARING STATEMENT

Not applicable.

PATIENT AND PUBLIC INVOLVEMENT

Patient research partners were involved in the design, conduct, reporting, and dissemination plans of this research.

PREVIOUS ABSTRACT PRESENTATIONS

The results of this study have been presented at the EULAR conference 2021.

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Supplementary table 1a

Key question on the value of imaging methods to guide interventional procedures

What is the efficacy / safety of [imaging technique] to guide interventional procedures (I) for outcome (O) at musculoskeletal sites of patients with RMDs (P), as compared to using [different technique] to guide interventional procedures (C)?	
Population	<p>Patients (no age restrictions) with RMDs undergoing an interventional procedure at (a) musculoskeletal site(s).</p> <p>“Patients with RMDs” are defined as patients with any rheumatic or musculoskeletal disease or discomfort (degenerative, inflammatory or autoimmune), also including for example patients with painful joints/muscles.</p> <p>Musculoskeletal sites are the following: joints, tendons, tendon sheaths, muscles, entheses, bursae, spine, soft tissue, nerves.</p>
Intervention	<p>[imaging technique]: US, CT, MRI, fluoroscopy/x-ray, fusion imaging.</p> <p>The intervention and comparator have to be different techniques (e.g. US (I) vs CT (C) or vs. palpation guidance (C)).</p>
Comparator	<p>[different technique]: no imaging guidance (e.g. clinical/palpation/anatomical orientated), or US, CT, MRI, fluoroscopy/x-ray, fusion imaging.</p> <p>The intervention and comparator have to be different techniques (e.g. US (I) vs CT (C) or vs. palpation guidance (C)).</p>
Outcome	<p>Differences in correct needle placement, patient and physician reported outcomes such as pain and function, safety/adverse events (e.g. infections, damage of surrounding tissue, hematoma, level of radiation), aspiration success (e.g. volume), yield of biopsy tissue, efficacy of treatment intention, costs, work productivity, need for repeated procedures, procedural tolerability, procedural feasibility.</p>

CT, computed tomography; MRI, magnetic resonance imaging; RMDs, rheumatic and musculoskeletal diseases; US, ultrasound

Supplementary table 2b

Key question on settings and technical standards for imaging guided interventions

<p>What is the efficacy / safety of [setting / technical standard] for imaging guided interventional procedures (I) for outcome (O) at musculoskeletal sites of patients with RMDs (P), as compared to not using [setting / technical standard] for imaging guided interventional procedures (C)?</p>	
<p>Population</p>	<p>Patients (no age restrictions) with RMDs undergoing an interventional procedure at (a) musculoskeletal site(s).</p> <p>“Patients with RMDs” are defined as patients with any rheumatic or musculoskeletal disease or discomfort (degenerative, inflammatory or autoimmune), also including for example patients with painful joints/muscles.</p> <p>Musculoskeletal sites are the following: joints, tendons, tendon sheaths, muscles, entheses, bursae, spine, soft tissue, nerves.</p>
<p>Intervention</p>	<p>Performing imaging guided interventions with a certain [setting / technical standard]:</p> <ol style="list-style-type: none"> 1. aseptic/antiseptic condition 2. assistance 3. monitoring vital signs 4. specific technical equipment <p>“Specific technical equipment” are for example specific US probes, needle with higher reflexion etc.</p>
<p>Comparator</p>	<p>Performing imaging guided interventions without the same/with a different [setting / technical standard]:</p> <ol style="list-style-type: none"> 1. aseptic/antiseptic condition 2. assistance 3. monitoring vital signs 4. specific technical equipment
<p>Outcome</p>	<p>Differences in correct needle placement, patient and physician reported outcomes such as pain and function, safety/adverse events (e.g. infections, damage of surrounding tissue, hematoma, level of radiation), aspiration success (e.g. volume), yield of biopsy tissue, efficacy of treatment intention, costs, work productivity, need for repeated procedures, procedural tolerability, procedural feasibility.</p>

RMDs, rheumatic and musculoskeletal diseases; US, ultrasound.

Supplementary table 3c

Key question on protocols for the conduction of imaging guided procedures

<p>What is the efficacy / safety of [procedural protocol] for imaging guided interventional procedures (I) for outcome (O) at musculoskeletal sites of patients with RMDs (P), as compared to not using [procedural protocol] for imaging guided interventional procedures (C)?</p>	
<p>Population</p>	<p>Patients (no age restrictions) with RMDs undergoing an interventional procedure at (a) musculoskeletal site(s).</p> <p>“Patients with RMDs” are defined as patients with any rheumatic or musculoskeletal disease or discomfort (degenerative, inflammatory or autoimmune), also including for example patients with painful joints/muscles.</p> <p>Musculoskeletal sites are the following: joints, tendons, tendon sheaths, muscles, entheses, bursae, spine, soft tissue, nerves.</p>
<p>Intervention</p>	<p>Performing imaging guided interventions with a certain [procedural protocol]:</p> <ol style="list-style-type: none"> 1. specific standard operational procedures 2. specific training for imaging guided interventions 3. imaging guided intra-target injections 4. contrast agent / air to control needle placement <p>“Specific operational procedures” are for example direct US guidance (I) vs US only to mark anatomical landmarks (C), or in plane (I) vs out of plane (C).</p> <p>“Intra target injections” means that the injection is guided to reach a specific anatomical area (e.g. intraarticular, tendon sheath, epineurium).</p>
<p>Comparator</p>	<p>Performing imaging guided interventions without the same/with a different [procedural protocol]:</p> <ol style="list-style-type: none"> 1. specific standard operational procedures 2. specific training for imaging guided interventions 3. imaging guided intra-target injections 4. contrast agent / air to control needle placement <p>Without “imaging guided intra-target injections” means that the injection is outside (extra-target) a specific anatomical area (e.g. extraarticular, tendon, endoneurium)</p>
<p>Outcome</p>	<p>Differences in correct needle placement, patient and physician reported outcomes such as pain and function, safety/adverse events (e.g. infections, damage of surrounding tissue, hematoma, level of radiation), aspiration success (e.g. volume), yield of biopsy tissue, efficacy of</p>

	treatment intention, costs, work productivity, need for repeated procedures, procedural tolerability, procedural feasibility.
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RMDs, rheumatic and musculoskeletal diseases; US, ultrasound

Supplementary table 4d

Outcome categories and respective outcome variables

Outcome categories	Possible outcome variables
Accuracy	accurate anatomical needle placement (accuracy), tissue/fluid acquired
Safety	adverse events, intra- and post-procedural pain, symptom severity
Efficacy	function, treatment response, time to next intervention, anatomical differences, electrophysiological parameter, treatment failure, quality of life, duration of therapeutic effects, pain medication, patient satisfaction
Cost/Time	costs (cost-effectiveness), time