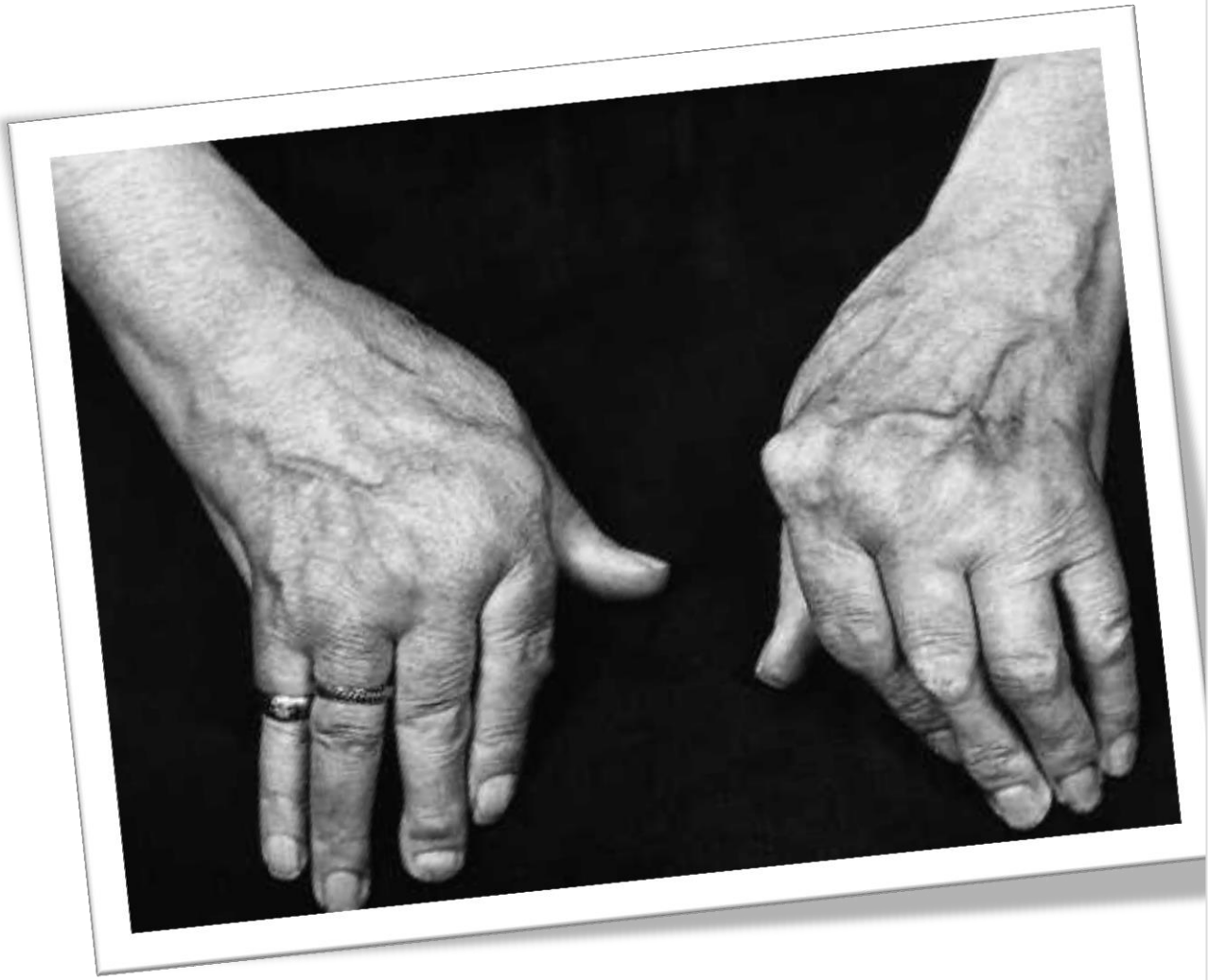
A Photoacoustic Instrument for diagnosis and monitoring of rheumatoid arthritis

A case study in the field of user involvement



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„Wege entstehen dadurch, dass man sie geht."
Franz Kafka

In an ideal world, decisions makers would base their decisions on the highest quality sources of scientific evidence that are available. During my study, I learned that reality is rather different from this ideal picture. A lot of time and money is wasted and wrong decisions are made. I therefore choose to write my thesis in the field of early Health Technology Assessment.

This thesis is a result of a half year of hard work. During the whole project, I experienced a lot and I gained new skills, insights and knowledge. A lot of people supported me during the execution of this project. I would like to thank some of them.

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I furthermore would like to thank my parents. Thank you for supporting me in every possible way and for encouraging me. Thank you for all the love you are giving to me. And – of course- thank you for the fireplace.

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ABSTRACT

INTRODUCTION: The role of technology in health care is getting increasingly important. Every year a huge number of medical devices are entering the health care market, with the goal to maintain and/or improve health through better diagnosis, treatment and monitoring. One emerging field in medical device development is the use of imaging technologies for diagnosis and monitoring of different diseases. This study focusses on a new imaging technology for diagnosis and monitoring of rheumatoid arthritis that is currently under development at the University of Twente.

AIM: Aim of this study is to access the potential of this new imaging technology for diagnosis and monitoring of rheumatoid arthritis in current and future health care settings.

METHOD: A needs assessment was conducted in an early phase of the development process of a new medical device for diagnosis and monitoring of rheumatoid arthritis. An analysis of guidelines and recommendations for rheumatoid arthritis in the United Kingdom, the Netherlands and Germany was performed. A SWOT analysis of MRI, Ultrasound, X-ray, CT scan and the new medical device was done, to identify advantages and disadvantages of the different imaging devices and identify possible needs. Importance of characteristics of imaging device for diagnosis and monitoring of rheumatoid arthritis and the performance of different imaging devices on these characteristics were established by a self-administered questionnaire.

RESULTS: Analysis of guidelines and recommendations in the Nederlands, the United Kingdom and Germany have shown that imaging devices are going to play a greater role in diagnosis and monitoring of rheumatoid arthritis. The care pathway is roughly the same in the three countries. However, guidelines differ in their recommendations about the areas of application of the different devices. Quantitative research among rheumatologists revealed that sensitivity, specificity and quality of the images are the most important characteristics for imaging devices. Least important characteristics were duration of scan and visualization of blood vessels. Qualitative research among rheumatologists showed that there is a great interest in devices that are immediately available when required and are easy to use. Furthermore rheumatologists are getting more aware of the need for early diagnosis. Rheumatologists wish to conduct faster measurements and quantitative measurements. Devices should be less complex and patient data about diagnosis and monitoring should be stored conform and centrally over time.

CONCLUSION: The new imaging technology that is under development at the University of Twente might play a part in the discovered issues of diagnosis and monitoring in rheumatoid arthritis, if test results indicate a good performance on characteristics that are perceived as important by rheumatologists and the device is less costly than MRI. More awareness of the importance of certain characteristics could lead to greater value of the device for its users. However, estimations are difficult to make, as the device is in such an early stage of development.

CONTENT

The health care market is subject to changes. Through new insights and developments from science, new possibilities for diagnosis, treatment and monitoring of different diseases are opening up. Furthermore there is an increasing demand for improved health care from society. A huge number of new technologies are developed each year and are entering the health care market.

The development of new technologies is one of the driving factors in rising health care costs. As can be seen from Figure 1, Drugs, Medical Devices and other medical advances contribute 22% of the overall increase in health care costs between 2001 and 2002.

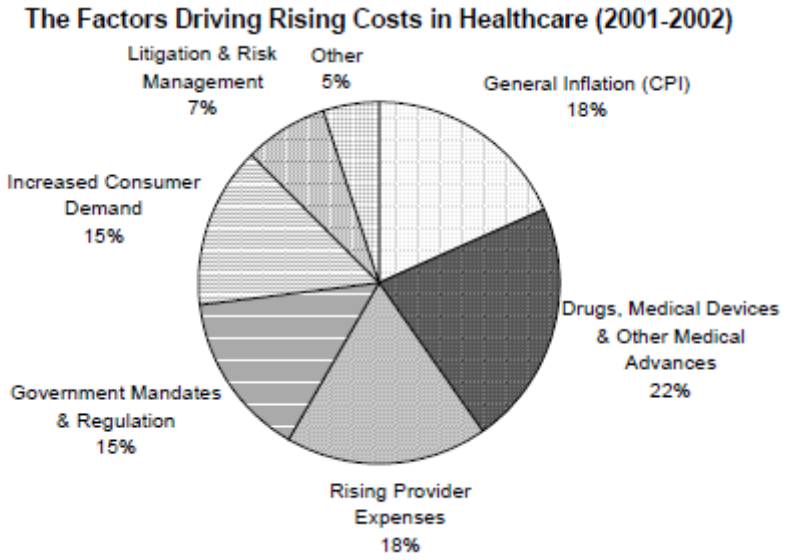


Figure 1: The Factors Driving Rising Costs in Health care (2001-2002) [1]

As in every other market, the resources available in the health care market are scarce[2]. Therefore resources need to be allocated carefully and different new technologies need to be traded against each other. According to Grimes [3], "some new technologies have clearly improved health and reduced costs, other have not". Decision-makers need to decide which new technology is worth adapting. During this process, they can make wrong decisions, which might lead to the adaption of an unnecessary technology or the rejection of a necessary technology (Figure 2).

		Dissemination: Adopted	Dissemination: Not adopted
Net value of innovation	Good	Appropriate use	Error of underdiffusion
	Bad	Error of overdiffusion	Appropriate nonuse

Figure 2: Dissemination and Net value of innovation [4]

Both cases are not desirable, as they can have bad consequences for health and health care. Overdiffusion might lead to the introduction of errors and adverse events. Error of underdiffusion might lead to an unfulfilled gap in the market [4].

HEALTH TECHNOLOGY ASSESSMENT

Health Technology Assessment (HTA) provides decision-makers with the ability to decide whether a medical device is worth adapting, considering social consequences in the short and long term [5-9]. HTA includes different aspects and research disciplines, such as medical effectiveness, cost expenses, organizational aspects etc. (Figure 3).

Figure 3: Different aspects of HTA [10]

Traditionally, HTA is applied after the first clinical use of a medical device. A device at this stage is already in prototype form and might even be on the market. Important targeting and design decisions have been made prior to this stage that influences the potential uptake of the design in the future.

Medical product development is a very complex process that starts with basic research on mechanisms and ends with (global) market access and pricing: In all these phases different stakeholders are playing a role and various decisions have to be taken when considering the diverse aspects in the assessment of new products. IJzerman & Steuten [11] developed a flowchart that presents the medical product development process and the uncertainty that surrounds it.

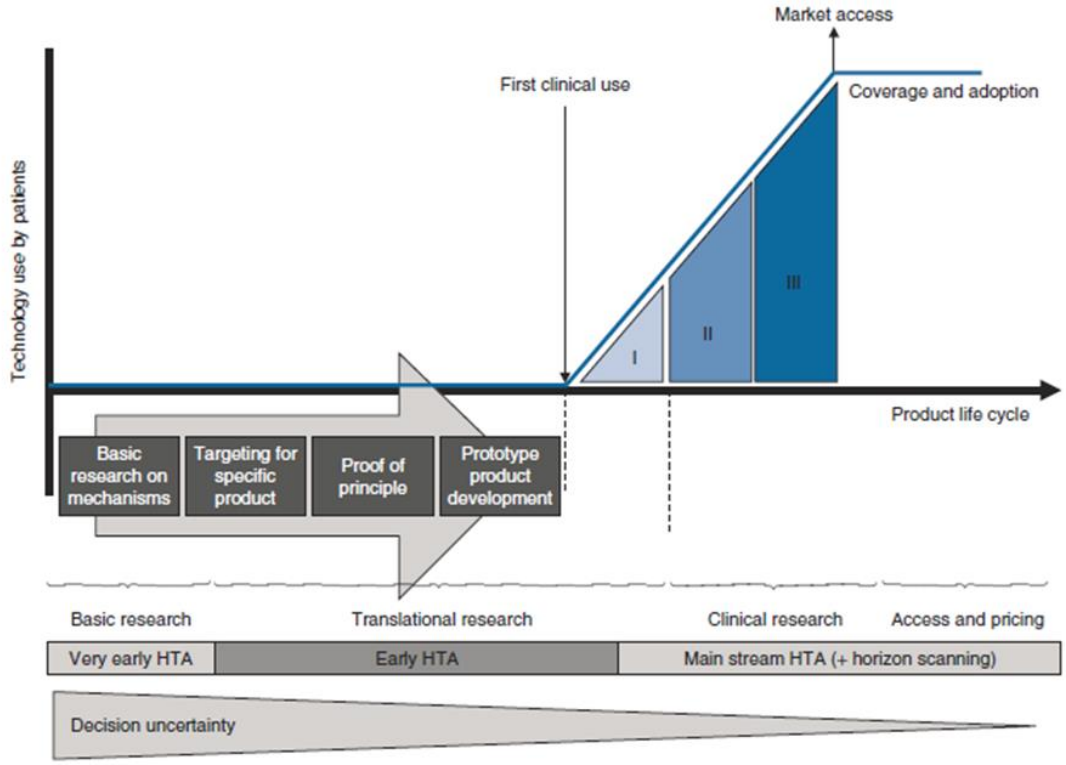


Figure 4: A simplified flowchart of the stages in medical product development

Four stages of medical product development can be distinguished: 1. Basic research, 2. Translational research, 3. Clinical research, 4. Access and pricing. In the early stages of the medical product development, uncertainty is high and mostly about the design and the performance of the product as well as uncertainty about future implementation of the device. During the medical product development path, the uncertainty about the design and the performance decreases, and uncertainty relates to market access, coverage and reimbursement decisions.

Although HTA is usually performed in later stages of medical product development, HTA can be performed in all four stages of medical product development. In Figure 4 a distinction between very early HTA, early HTA and main stream HTA plus horizon scanning is made. In recent years, earlier assessment has gained momentum.

Lately governments and industries have shown an increased interest in the assessment of new products in earlier stages of medical product development. It is a result of an increased pressure to maximize the revenues of the investments in medical product development [12]. The performance of HTA in an earlier stage of the medical device development process – early HTA – can help to prevent (costly) failures of a technology and (at that stage) difficult adjustments [13]. Through early HTA government and industry can identify the devices that are most likely to generate value for money. Manufacturers also seek to steer their research and development (R & D) more effectively. Early HTA includes the assessment of (likely) safety, effectiveness, cost effectiveness, market size, patient needs, barriers and facilitators and product specifications[11, 14]. Early HTA gives decision support on technology design and strategic management for developers and investors. Because early HTA takes place before first clinical use, the available evidence is based on prototype testing, animal studies, expert opinions and outcomes from similar technologies[15].

In early stages of development of medical devices the focus set by the developers is mostly on technical development.

"We ourselves are currently primarily looking at the technological side of the device" - [16]

However, the success of the medical device to the company is determined by whether there is actually a market for the device in health care. Ultimately, whether the end-user is willing and able to use the device and actually benefit from it is determined by the need for the device.

AIMS AND OBJECTIVES OF THIS STUDY

At present, at the University of Twente, a Photoacoustic Imager for diagnosis and monitoring of rheumatoid arthritis is being developed. We aim to evaluate this device (Box 1).

The medical device is currently in the prototype product development stage, which is in phase two of the flowchart presented in Figure 4: translational research. The device has not been applied in a clinical setting yet and no clinical trials with patients have been performed. The clinical potential of the device is thus undetermined.

Different decision problems occur in the prototype product development stage. The industry needs to make a decision on whether or not to invest in further R & D and to decide on marketing the product. The government needs to decide if they should invest in the new medical device in order to stimulate economic growth and gain health benefits. Clinical and basic research centers are addressing questions about the research focus and the fit of the project in their portfolio.

For the Photoacoustic Imager it is not clear where the medical device should be implemented. At present, it is unknown whether potential users of the medical device have a need for a novel diagnostic and monitoring tool for rheumatoid arthritis, and what the relative advantage of the Photoacoustic Imager is.

RESEARCH QUESTION

The main research question of this thesis is:

What is the potential of the Photoacoustic Imager for the diagnosis and monitoring of rheumatoid arthritis in current and future health care settings?

In order to answer the main research question, the following subquestions need to be answered:

1. What is the current care pathway of rheumatoid arthritis?
- 1.1. Which imaging devices are playing a role in diagnosis and monitoring of rheumatoid arthritis?
- 1.2. What are advantages and disadvantages of the different imaging devices?

2. What is the appropriate place for the Photoacoustic Imager in the care pathway?
- 2.1. What are the main problems in diagnosis and monitoring of rheumatoid arthritis?
- 2.2. What are trends and changes in diagnosis and monitoring of rheumatoid arthritis?

3. What are user needs in diagnosis and monitoring of rheumatoid arthritis?
- 3.1. What are important characteristics of diagnosis and monitoring devices for rheumatoid arthritis?
- 3.2. What are user's opinions about characteristics of current devices?

Box 1: Confidential

METHOD

SWOT –ANALYSIS

A SWOT analysis was performed for RAPACT and its (main) competitors (MRI, CT-scan, X-ray, Ultrasound) to identify strength, weaknesses, opportunities and threats of the devices. An overview of the different imaging devices and their advantages and disadvantages was made. Furthermore information about future developments in the field of diagnosis and monitoring of rheumatoid arthritis, which might stimulate or hinder the diffusion of the devices were identified.

To identify advantages, disadvantages, trends and changes in diagnosis and monitoring of rheumatoid arthritis, Google Scholar, PubMed, Web of Science and Scopus were searched, with the keywords "diagnosis", "monitoring", "rheumatoid arthritis", "trends", "changes", '"opportunities", "shift", "adjustment", "advance", "modification", "innovation" , '"imaging devices", "MRI", "Ultrasound", "X-ray", "CT-scan", "advantages", "disadvantages" which were used in different combinations. Furthermore the references of selected papers were checked for other related research. References of interest were selected through scanning the titles. When the title seemed of interest, the abstract of the article was scanned. A reference was considered for further investigation when the keywords appeared.

Pathways and guidelines for diagnosis and monitoring of rheumatoid arthritis in the Netherlands, the United Kingdom and Germany were examined and checked upon (recent) changes. The pathways and guidelines have been investigated with a special focus on the role imaging technologies are playing in these pathways/guidelines.

USER RECRUITMENT AND DATA COLLECTION

A self-administered questionnaire was developed with the online software tool Survey Monkey (Appendix G). Target group of the questionnaire were rheumatologists from the Netherlands, the United Kingdom and Germany. Respondents for the questionnaire were reached through the online newsletter of the British Society for Rheumatology and E-Mails provided by the researcher to different hospitals and rheumatologists. Data collection was performed from August 2013 until September 2013. Pilot testing was performed in July 2013 with two experts in the field of early HTA, a rheumatologist and a Health Sciences student. A total of 38 rheumatologists from the Netherlands, the United Kingdom and Germany participated in the questionnaire.

SELF-ADMINISTERED QUESTIONNAIRE

The self-administered questionnaire was structured in five parts.

The first part was about diagnosis and monitoring of Rheumatoid Arthritis. Aim of this part was to examine if rheumatologists use imaging devices for diagnosis and monitoring of rheumatoid arthritis, and if yes, which devices they are using, how important 10 different characteristics of imaging devices are and how satisfied rheumatologists are with these 10 characteristics with regard to different imaging devices. The characteristics were identified through literature study and consultation of a rheumatologist. The characteristics identified were: Sensitivity, Specificity, Quality of the images, Duration scan, Assessment of big joints, Visualization of blood vessels, Visualization of damaged bone and cartilage, Visualization of tendons and ligaments, Subjective quantification of effect of therapy and objective quantification of effect of therapy. The

importance of the 10 characteristics was assessed through five point Likert type scales. Rheumatologists were asked to indicate on a five point Likert type scale how satisfied they are with the imaging devices they are using for diagnosis and monitoring of rheumatoid arthritis. Furthermore a question about problems that might encounter in using imaging devices for diagnosis and monitoring of rheumatoid arthritis was asked.

In the second part the concept "future developments in rheumatoid arthritis" was assessed by asking respondents to come up with the most important future developments in diagnosis and monitoring of rheumatoid arthritis.

In the third part future trends and important characteristics that might not been included in the first part of the questionnaire were assessed by asking rheumatologists to indicate three changes in diagnosis and monitoring of rheumatoid arthritis and to describe the ideal diagnostic and the ideal monitoring tool.

The fourth part introduced the medical device from the case study. In the fourth part opposing adjectives were used to examine how important the advantages and disadvantages of the device would be, how large participants estimate the additional value of the device for their daily practice and how they estimate the future demand for the device. In the fifth part data about background information (years of experience and number of patients per month) was gathered.

The self-administered questionnaire contained open-ended and closed-ended questions. The open-ended questions were used to validate and embellish the quantitative survey findings [17]. Concepts that are ambiguous were defined in the questionnaire to avoid misunderstanding.

The qualitative data was analyzed with a technique called coding. For coding of the qualitative data the software program Atlas.ti was used. The first step during this analysis was open coding. All qualitative data was used to identify similarities and differences and make an initial classification and labeling of the different concepts found. After the open coding all data was reanalyzed to identify important, general concepts of the data (axial coding)[18, 19].

The quantitative analysis of the self-administered questionnaire was performed using SPSS software version 20 and Excel 2010. Basic statistics (frequency, mean, mode, variance and standard deviation) were determined for background information.

The answers to the Likert type scale questions in the questionnaire were allocated numbers/a score, assuming a linear relation, with 5 points for the most positive answer (Very important/ Very satisfied) and 1 point for the least positive answer (Very unimportant/ Very dissatisfied). Weighted averages of these answers were calculated in order to identify the most important criteria and which criteria scored best with regard to satisfaction for each device. Ranges, mode, minimum and maximum were calculated for the importance and the satisfaction of the different criteria (Appendix F). Furthermore the overall satisfaction of all criteria was calculated per device.

RHEUMATOID ARTHRITIS

Rheumatoid arthritis (RA) is a chronic autoimmune disease that affects the joints of the wrist and fingers. It causes pain, swelling, stiffness and loss of function in the joints [20, 21]. Furthermore many other organs can be affected, causing for example severe lung fibrosis. Rheumatoid arthritis is associated with an increased prevalence of coronary artery disease and an increased risk of premature mortality[22]. The symptoms vary from person to person, and even per day. It begins between the ages of 30 and 60; men get it mostly later in life than women [23].

PATHOPHYSIOLOGY

In rheumatoid arthritis, the joints that are lined with synovium are affected the most. Small joints of the hands and feet are affected, mostly with symmetrical distribution.

Rheumatoid arthritis is an autoimmune disease; this means that antibodies in the human body are attacking the tissues in the joint. If the synovial membrane is attacked by antibodies (activated white blood cells), it gets inflamed. In a healthy person, the synovial membrane is a thin layer. In an inflamed joint, the antibodies lead to a thickening of the synovial membrane (pannus). Furthermore blood vessels might be inflamed. The thickened synovium membrane (pannus) leads to the destruction of cartilage and bone in the joint. Tendons and ligaments in the joint are weakened. As a result, the joint gets unshaped/bulky (Figure 6) [20, 24-26].

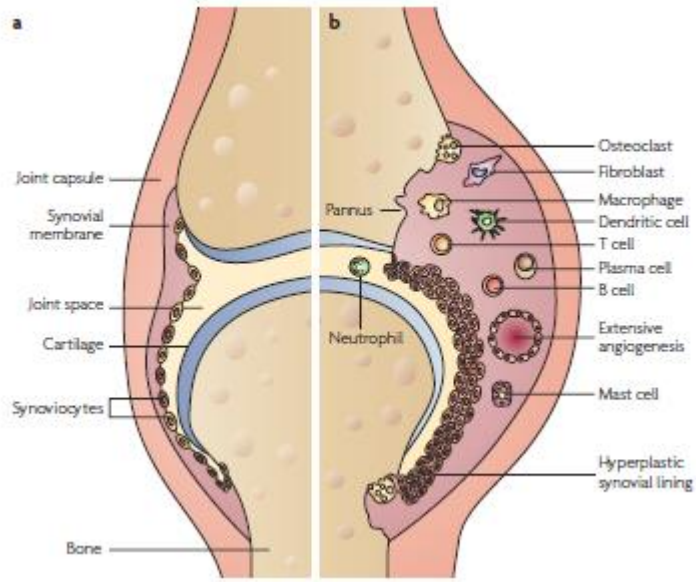


Figure 6: Schematic overview of a normal joint (a) and a joint affected by rheumatoid arthritis (b) [27]

The care pathway of patients with rheumatoid arthritis is roughly the same for the Netherlands, the United Kingdom and Germany.

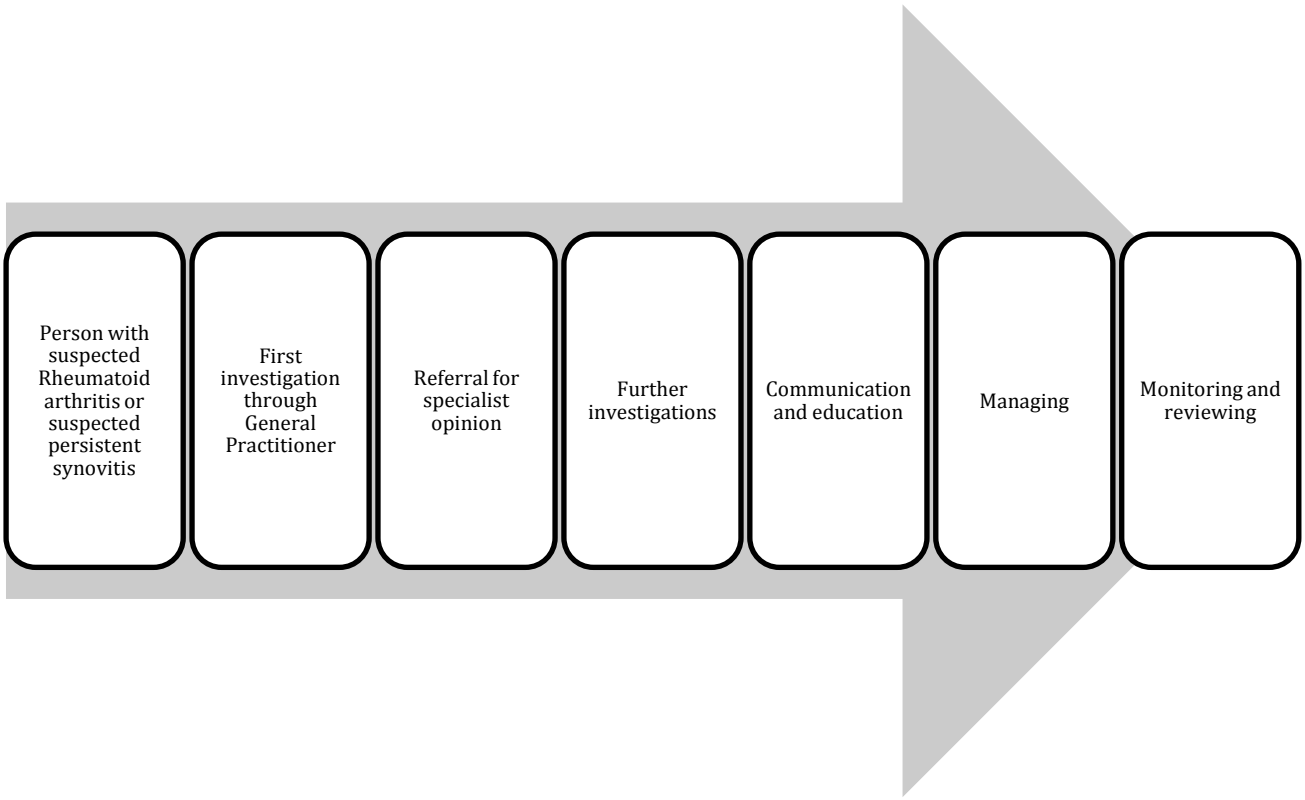


Figure 7: A schematic, simplified care pathway of rheumatoid arthritis [28]

The first contact point for a person with suspected rheumatoid arthritis or suspected persistent synovitis is normally the General Practitioner. The General Practitioner makes the first physical investigation and anamnesis of the patient. In the Netherlands and the United Kingdom, the General Practitioner has a gatekeeping function to restrict access to secondary care[29, 30]. After the initial diagnosis of rheumatoid arthritis the patient is referred to a rheumatologist. Diagnosis of rheumatoid arthritis is based on clinical, laboratory and imaging tests[31].

There are differences in the guidelines of the United Kingdom, the Netherlands and Germany about when to assume suspected rheumatoid arthritis and when the patient should be referred to a rheumatologist (Figure 8).

	United Kingdom	The Netherlands	Germany
Symptom Duration	≥ 3 weeks	≥ 3-4 weeks	≥ 6 weeks
Morning Stiffness	≥ 30 minutes	≥ 30 minutes	≥ 60 minutes
Synovitis	≥ 1 joint	≥ 1 joint	≥ 2 joint regions
Time Frame referral	Within 3 working days of presentation	Patients with symmetrical arthritis in three or more joints should visit a rheumatologist within 2 weeks.	Within 2 weeks
Other/ Additional	There has been a delay of ≥ 3 month between onset of symptoms and seeking medical advice	Pressure pain at the metacarpophalangeal joints (MCP's) or metatarsophalangeal joints (MTP's)	

Figure 8: Referral differences in the United Kingdom, the Netherlands and Germany [22, 32, 33]

The guidelines are mostly in line with the recommendation of the European League Against Rheumatism (EULAR), which states that "Arthritis is characterised by the presence of joint swelling, associated with pain or stiffness. Patients presenting with arthritis of more than one joint should be referred to, and seen by, a rheumatologist, ideally within six weeks after the onset of symptoms" [34]. It should be noted that these criteria are no diagnostic criteria for rheumatoid arthritis. The classification criteria might serve as a guide for the diagnosis. This leads to differences within and between countries about guidelines and their adherence. See appendix B for the complete list of recommendations.

All guidelines also refer to the American College of Rheumatology (ACR) and EULAR classification criteria for rheumatoid arthritis.

After the definitive diagnosis of rheumatoid arthritis, the patient needs to be informed about the disease and further management. The disease needs to be monitored in order to chart disease progression and determine appropriate treatment. Monitoring and evaluation of rheumatoid conducted subjectively and through laboratory and/or imaging tests. To measure disease activity and functionality, different measurement methods can be applied, such as the ACR criteria, the ACR response criteria, ACR remission criteria, the health assessment questionnaire (HAQ), the rheumatoid arthritis disease activity index (RADAI), disease activity score (DAS), radiologic progression (Sharp and Larsen method), WHO-ILAR core set, EULAR OMERACT – RAMRIS, the simplified disease activity index (SDAI) and the clinical disease activity index (CDAS). For an overview of the different methods to measure disease activity and functionality, see appendix A.

MAIN PROBLEMS IN DIAGNOSIS AND MONITORING OF RHEUMATOID ARTHRITIS

One of the main problems of diagnosis in rheumatoid arthritis is that there are no disease-specific diagnostic features, because not all patients with rheumatoid arthritis have a clear clinical picture and the range of symptoms and its characteristics vary per patient and stage of disease[35].

It is suggested that diagnosis and referral of rheumatoid arthritis in an early stage of the disease is very important in order to prevent joint damage, achieve better disease control and improved outcomes in terms of lost productivity. [36-41].

At present, there is a long lag time between symptom onset and first definite diagnosis. Many factors contribute to this lag time.

1. **Access issues:** Access to a specialist is difficult because there are not enough rheumatologists for the number of patients. In 2006, 579 rheumatologists were working in Germany but the German Society for Rheumatology stated that 1350 rheumatologists are needed, which is a shortcoming of 771 rheumatologists [42]. To overcome existing demand and fulfill future demand, the number of rheumatologists that is in education must be considerably raised [43].
2. **Financial issues:** The time consuming monitoring and diagnosis is not sufficiently reimbursed, which can result in treatment delay of anti-rheumatic drugs [44, 45].
3. **Patient's perception:** Patients wait too long before seeking medical advice because they do not recognize the gravity of the situation [46, 47].
4. **Physician's confidence and expectation:** A low perception of the specialist's competence and/or high confidence of the General Practitioner are linked to nonreferral to a specialist [48-53].
5. **Skills:** Diagnosis of early rheumatoid arthritis is often difficult for the General Practitioner [50, 53].
6. **Definitions:** To complicate the diagnostic process, there is no consensus among rheumatologists about the definition of "early rheumatoid arthritis". A study by Aletaha et al. (2002) among 42 rheumatologists revealed that 37.2% use the term early rheumatoid arthritis if the symptom duration is less than three months, and about 30.2 % if the symptom duration is less than six months, which shows that there are still rheumatologists who do not define early rheumatoid arthritis in line with guidelines, recommendations and studies [54-56].

As mentioned earlier, diagnosis and referral in early rheumatoid arthritis can improve outcomes significantly. With regard to the earlier mentioned lag time between symptom onset and first definite diagnosis, improvement of the referral process is needed.

Another issue about diagnosis and monitoring of rheumatoid arthritis concerns registry of data on patients with rheumatoid arthritis. National registers do not exist or do not cover all patients. This results in uncertainty about the number of diagnosed patients, the professional who made the diagnosis, in what timeframe the diagnosis was made, which therapy is applied and with what success. This makes it more difficult to monitor different treatment approaches and follow-up of patients [57].

Through the whole care pathway, imaging devices are used for diagnosis and monitoring of rheumatoid arthritis.

In 2013, the EULAR gave recommendations for the use of imaging of the joints in the clinical management of rheumatoid arthritis (Figure 9).

EULAR recommendations
When there is diagnostic doubt, CR, ultrasound or MRI can be used to improve the certainty of a diagnosis of RA above clinical criteria alone.
The presence of inflammation seen with ultrasound or MRI can be used to predict the progression to clinical RA from undifferentiated inflammatory arthritis.
Ultrasound and MRI are superior to clinical examination in the detection of joint inflammation; these techniques should be considered for more accurate assessment of inflammation.
CR of the hands and feet should be used as the initial imaging technique to detect damage. However, ultrasound and/or MRI should be considered if conventional radiographs do not show damage and may be used to detect damage at an earlier time point (especially in early RA).
MRI bone oedema is a strong independent predictor of subsequent radiographic progression in early RA and should be considered for use as a prognostic indicator. Joint inflammation (synovitis) detected by MRI or ultrasound as well as joint damage detected by conventional radiographs, MRI or ultrasound can also be considered for the prediction of further joint damage.
Inflammation seen on imaging may be more predictive of a therapeutic response than clinical features of disease activity; imaging may be used to predict response to treatment.
Given the improved detection of inflammation by MRI and ultrasound than by clinical examination, they may be useful in monitoring disease activity.
The periodic evaluation of joint damage, usually by radiographs of the hands and feet, should be considered. MRI (and possibly ultrasound) is more responsive to change in joint damage and can be used to monitor disease progression.
Monitoring of functional instability of the cervical spine by lateral radiograph obtained in flexion and neutral should be performed in patients with clinical suspicion of cervical involvement. When the radiograph is positive or specific neurological symptoms and signs are present, MRI should be performed.
MRI and ultrasound can detect inflammation that predicts subsequent joint damage, even when clinical remission is present and can be used to assess persistent inflammation.

Figure 9: Recommendations EULAR [58]

In the EULAR recommendations for the management of early arthritis ultrasound, power Doppler and MRI are regarded as helpful tools in addition to clinical examination in doubtful cases. Furthermore radiographs are recommended as a method to assess structural damage of the hands and feet every 6 to 12 months during the first years [34].

However, use and perceived use of imaging devices in the care pathway differs among countries.

According to the guideline “Diagnostiek en behandeling van reumatoïde artritis”of the Dutch Association of Rheumatology [32] X-ray is of little importance in diagnosis of rheumatoid arthritis. Reason for this is that negative findings of an X-ray do not exclude the disease. However, in a later stage of the disease, X-rays are important for evaluation of disease progress. The guideline furthermore recommends the use of MRI if there is suspicion of osteonecrosis. Besides that, no other imaging devices are mentioned in the guideline.

In the National clinical guideline for management and treatment of adults with rheumatoid arthritis in the United Kingdom the limited use of X-ray in the early stages of rheumatoid arthritis is also recognized. However, X-rays of the hands and feet are considered as helpful in early (persistent) synovitis, because erosive damage can be detected despite all other tests being normal. In this consideration it is also taken into account that x-rays are a "readily accessible base-line for future determinations of disease progression". The guideline states that ultrasound and small joint MRI might replace X-rays in the future if they become more widely available and the importance of early inflammatory and erosive changes becomes more apparent, but that X-ray remains the golden standard. The guideline only recommends an urgent MRI scan in case of suspicion of cervical myelopathy [22].

In the guideline of the German Society of Rheumatology, are x-rays of the right and left hands and feet an essential part of the primary diagnosis. However they state that x-rays are of no use in early rheumatoid arthritis. X-rays are only useful to exclude bone fractures. Ultrasound (including Power Doppler) and MRI are perceived as methods that can detect structural joint and bone changes as well as joint effusion earlier than x-rays. MRI and Scintigraphy are perceived as useful for a better presentation of changes in the bone metabolism. Power Doppler Ultrasound and MRI are perceived as the best methods to detect early signs of reversible structural changes of rheumatoid arthritis like an increased vascularization of the proliferated synovium and bone narrow oedema. However it should be noted that MRI is not routinely performed [33].

SWOT ANALYSIS

In order to access the advantages and disadvantages of the different imaging devices, as well as possible pitfalls and opportunities on the market, a SWOT analysis was performed. The analysis was performed with a focus on rheumatoid arthritis. The complete SWOT analysis tables are displayed in Appendix D.

MRI

Magnete Resonance Imaging (MRI) is a well-established technology that is mostly used in monitoring of rheumatoid arthritis. MRI could also be used in diagnosis to improve certainty of the diagnosis. The images MRI provides give a good overview of the articular surfaces and internal bone structure. Synovitis, Bone Marrow Oedema, Cartilage, ligaments, tendons and tendon sheaths as well as intra- and extra- articular fluid collections can be assessed. MRI is painless but some patients might feel uncomfortable, as a scan takes 15-90 minutes and there is a risk of getting claustrophobic. Furthermore the use of contrast dye could harm patients. Another disadvantage of MRI is that it is costly and not widely available, which causes long waiting lists and a long time between the scan and receiving of results. In comparison with Ultrasound the resolution of MRI is low and there is the problem of Motion Artifacts. Furthermore wrist, MCP, PIP and DIP joints cannot be examined with equal high resolution at the same time and these measures would also be too time consuming and expensive. Imaging of cartilage in small joints with adequate resolution remains a problem. Interpretation of the images is rather complex and depends highly on the skills of the operator.

MRI can be used in 1st and 2nd line. Especially in 2nd line to certify a diagnosis and to monitor disease activity, MRI gets more and more recognized as a valuable device. New forms of MRI like small joint MRI might be used in 1st line, as they require less physical space and are less costly than MRI. Disadvantages of these low- field extremity MRIs are that imaging clarity might be lower than conventional MRI and have a limited spatial resolution. It is less sensitive to oedema and contrast dye is required to identify synovitis [59, 60]. Techniques like gadolinium - enhanced MRI might be useful to access cartilage damage and monitor therapeutic effects on cartilage integrity[61, 62]. Diffusion – weighted MRI is a technique that also might be more used in the future, as it is contrast free. It visualizes osseous(bone tissue) and soft tissue oedema[63, 64]. 3D MRI might be useful to detect soft tissue lesions and early erosions[65]. 3D MRI sequences with isotropic voxels reduce the duration of the scan while beholding image quality[66]. Data obtained via MRI can be stored and read centrally, what might get important in order to build an (inter-) national database and for later retrieval in order to evaluate prognostication. An additional opportunity for MRI is that MRI is affiliated in different recommendations and guidelines, which might stimulate its usage.

Threats to MRI (and every other device) are other established devices or new devices that are entering the market and might be better and cheaper than MRI.

ULTRASOUND

In contrast to MRI, Ultrasound is a widely available technology that can be used in diagnosis and monitoring of rheumatoid arthritis. Ultrasound is non-invasive and no ionizing radiation is used. Another advantage is that it is painless and can be conducted interactive with the patient in real time. It takes approximately 15-45 minutes to gather the data needed. Ultrasound can be used to assess thickening of the synovial membrane, bursae or tendon sheaths and/or synovial blood flow. Furthermore fluid in joints, bursae and tendon sheaths can be observed. However, interpretation of the images is complex and highly dependent on the operator. The inter observer variability is high and there are problems with reproducibility. Data gathered can be recorded but what should be documented is often subjective, which makes it difficult to compare data. Another disadvantage is that the quality of the images is site dependent. In addition, internal bone structure is not visualized what makes it difficult to access changes in the bone and identify e.g. bone marrow oedema. There is uncertainty about the relative advantage of Ultrasound over X-ray in showing erosive progression and there are only few tests on systems in longitudinal follow-up studies done.

Ultrasound can be used in 1st and 2nd line and can be used in imaging studies or to guide invasive joint procedures. An opportunity for Ultrasound might be the development of a global ultrasound score in order to examine the extend of synovitis[67]. Ultrasound might help to identify poor prognostic factors in rheumatoid arthritis and is itself a helpful tool for prognostication of disease [68, 69]. Use of portable ultrasound machines might make appointments with radiologists unnecessary[70]. Like MRI, Ultrasound usage might be stimulated through recently published guidelines/recommendations who emphasise the role of Ultrasound as a detection tool for inflammation in (early) rheumatoid arthritis.

X-RAY

X-ray is seen as the “gold standard” for diagnosis of rheumatoid arthritis and there are validated assessment methods available. In later stages of the disease X-ray can detect changes in joint space and bone erosion. However, X-rays need to be performed by a radiographer in a radiology department, which limits the access. A big disadvantage of x-ray is that it uses radiation, which is harmful for the body. X-rays are useful to differentiate rheumatoid arthritis from other joint conditions like e.g. osteoarthritis. X-rays are most useful for assessment of signs of rheumatoid arthritis in later stages. Soft tissue changes and early bone erosion cannot be visualized in early stages. X-rays are also not good for identifying non-progressors. A big advantage of x-ray is that standardized and blinded centralized reading of the data is possible. Although X-ray is seen as the “gold standard”, the Dutch guideline for diagnosis and monitoring of rheumatoid arthritis gives and advice against the usage of X-ray.

CT SCAN

CT scan is a technology rarely used in clinical practice, although the images displayed are clearer than standard x-ray and more sensitive to bone erosions than MRI. Reasons for this are the disadvantages of a CT-scan. First of all, radiation and the use of contrast dye make the technology less safe than other technologies. It has a low sensitivity to soft tissue changes in comparison with MRI and Ultrasound, and these soft tissue changes are extremely important in the diagnosis of rheumatoid arthritis. CT scans is performed in special centres and the time between scan and results is long.

New forms of the CT scan might play a role in monitoring of rheumatoid arthritis. Examples are integrated PET/CT machines, which can be used in rheumatology to diagnose and monitor large vessel vasculitis, a complication of rheumatoid arthritis[71]. Multi – detector computerized tomography scans (MDCT scan), can be used to make three – dimensional images of the joints[72, 73].

Box 2 : Confidential

According to an exploratory process report of the European Commission health care should be focused on prevention, early/accurate diagnosis and effective treatment[74]. This approach/development can also be observed in the area of diagnosis and monitoring of rheumatoid arthritis.

Early diagnosis of rheumatoid arthritis has gained greater significance and attention in the last years. As a result the American College of Rheumatology developed new classification criteria for rheumatoid arthritis in 2010, where the focus is on the early stages of the disease[75].

As mentioned before, there is a rising awareness for early diagnosis and (more) effective treatment. This development is caused by the insight that early treatment approaches gain the most benefits for patients and could even increase the chance of remission. This timeframe is often referred to as the "window of opportunity" [76-79].

Not only early diagnosis, but also close monitoring of patients has gained greater interest in the past years. Continuous monitoring of patients and adjustment of the care they need by a rheumatologist leads to improved outcomes [80, 81]. In 2010 recommendations to treat rheumatoid arthritis to target have been made. These recommendations reflect the trend of continuous monitoring. Validated composite measures of disease activity should be implemented in routine clinical practice, in combination with structural changes and functional impairment[82].

Looking for long term outcomes in rheumatoid arthritis is another new thought in the field of rheumatology. According to a study of van der Linden et al. (2010) patients with a delay longer than 12 weeks have worse disease outcome (rate of joint destruction and DMARD-free remission) compared with patients with a delay less than 12 weeks[79].

These developments have led to an increased interest in imaging devices and how they can be of use for the new developments (Figure 10).

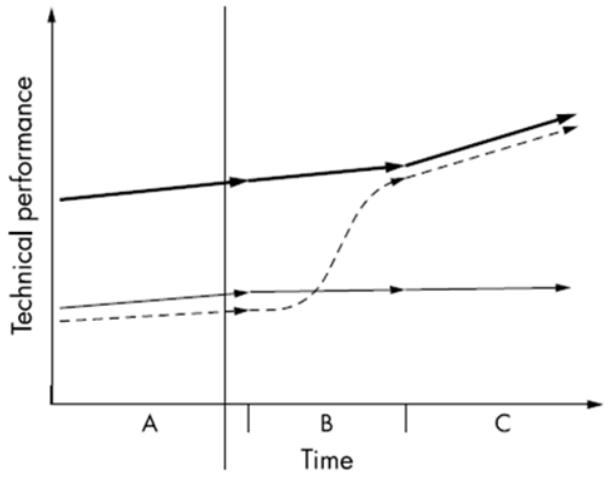


Figure 10: Technical demand – performance relationship [83]

41 respondents filled in the self-administered questionnaire. One was excluded from the questionnaire, because only three questions were answered, two were excluded because they completed the survey in less than two minutes, which leaves 38 respondents. The average time to complete the survey was 16 minutes with a standard deviation of 15:00 minutes. 5% completed the survey in English, 29% in German and 66% in Dutch. The average years of experience for all rheumatologists are 18 years with a standard deviation of seven years. The average number of patients per month is 127 with a standard deviation of 88 patients.

Of the 38 respondents, 29% stated that they do have problems with the devices they are using and 71% stated that they do not experience problems with the imaging devices they are using for diagnosis and management of rheumatoid arthritis. However, 61% of all respondents expressed a need for higher quality tools in diagnosis and monitoring of rheumatoid arthritis.

The problems with currently available devices the respondents mentioned are divers, but sensitivity and specificity of the devices are mentioned often. Other problems mentioned are the costs of the device, the time a scan takes, the inability to make reproducible images (positioning problems X-ray), a lack of objective measurements and possibilities for differentiation, and the inability to display certain structures like erosion or early inflammation. Many of the problems are not specific for one device, but occur in most of the devices.

Most rheumatologists are using two devices (42.11%) for diagnosis and monitoring of rheumatoid arthritis. Only a minority (10.53%) use just one device.

In the United Kingdom, MRI, Ultrasound and X-ray are used equally. In Germany X-ray and Ultrasound are used the most, followed by MRI. In the Netherlands X-ray and Ultrasound are used most often. Two respondents in Germany also stated that they sometimes make use of scintigraphy.

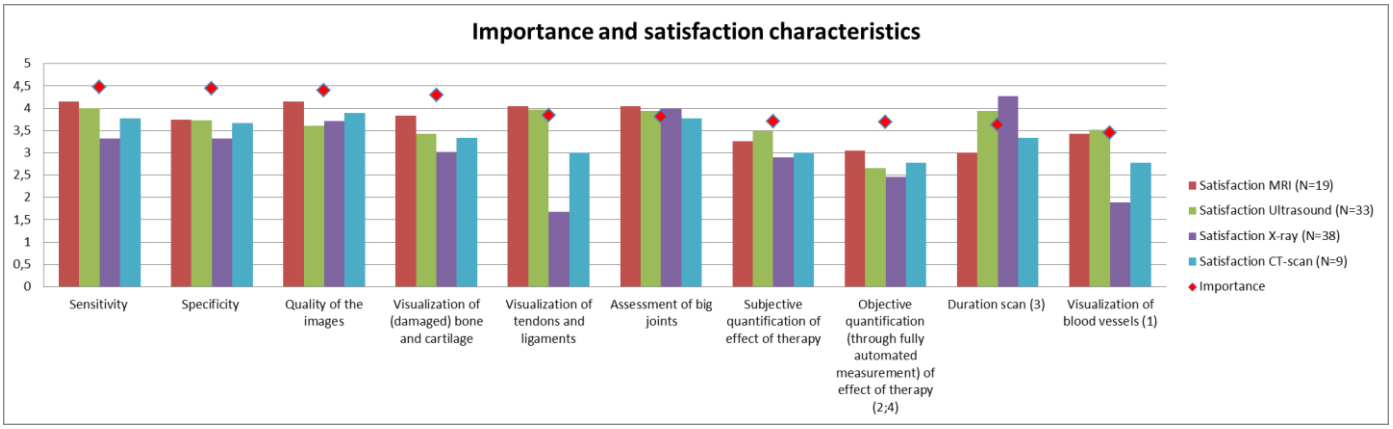
With regard to the importance of characteristic for imaging devices to diagnose and monitor rheumatoid arthritis, sensitivity and specificity are the most important characteristics rated by the rheumatologists, followed by quality of the images and visualization of (damaged) bone and cartilage. The least important characteristic is visualization of blood vessels (Figure 11).

Characteristic	Importance
Sensitivity	4.47
Specificity	4.45
Quality of the images	4.39
Visualization of (damaged) bone and cartilage	4.29
Visualization of tendons and ligaments	3.84
Assessment of big joints	3.82
Subjective quantification	3.71
Objective quantification	3.68
Duration scan	3.63
Visualization of blood vessels	3.45

Figure 11: Importance of characteristics for imaging devices to diagnose and monitor rheumatoid arthritis based on the results of the questionnaire (N= 38)

Figure 12 shows the weighted average of the importance of the characteristics and the satisfaction with the characteristics from most to least important. Due to incomplete responses some weighted averages of the satisfaction were calculated using smaller sample sizes (visualization of blood vessels and objective quantification of effect of therapy in Ultrasound, duration of scan and objective quantification of effect of therapy in X-ray). The red dots indicate the importance of each characteristic. The dark red bars show the satisfaction with the characteristics of MRI, the green bars show the satisfaction with the characteristics of Ultrasound, the purple bars show the satisfaction with the characteristics of X-ray and the light blue bars show the satisfaction with the characteristics of CT-scan. MRI performs best on sensitivity, specificity, quality of the images, assessment of big joints, visualization of (damaged) bone and cartilage, visualization of tendons and ligaments and objective quantification (through fully automated measurement) of effect of therapy. For the characteristic duration of scan, X-ray scores best, for subjective quantification of effect of therapy and visualization of blood vessels, ultrasound scores best.

With regard to sensitivity, specificity, quality of the images, visualization of (damaged) bone and cartilage, subjective and objective quantification of effect of therapy, the performance of all devices is lower than the importance, showing that there is potential for improvement.



(1) N Ultrasound = 32, (2) N Ultrasound = 32, (3) N X-ray = 37, (4) N X-ray = 37

Figure 12: Weighted average of the satisfaction with different imaging devices and their importance based on the results of the questionnaire

Overall satisfaction with MRI is high, with respondents stating in 11% of all cases that they are very satisfied, 52.6% of all cases that they are satisfied, 29.5% of all cases that they are neither satisfied nor dissatisfied, 6.3% of all cases dissatisfied and only 0.5% of all cases very dissatisfied. Rheumatologists are most satisfied with the characteristics Sensitivity and Quality of the images in MRI, with a weighted average of 4.2 each. Rheumatologists are least satisfied with the performance of MRI on the duration of scan (weighted average 3.0) and the ability of MRI to perform objective quantification (weighted average 3.1). Rheumatologists scored subjective and objective quantification, duration scan and visualization of blood vessels with a weighted average beneath 3.5, which indicates that they are not satisfied with the performance of the device on these characteristics, but these characteristics are also the least important ones according to the questionnaire.

Respondents are overall very satisfied in 12.8% of all cases with the performance of Ultrasound on the different characteristics. In 47.9% they are satisfied, 30.8% neither satisfied nor dissatisfied, 7.6% dissatisfied and 0.9% very dissatisfied. Rheumatologists are most satisfied with the characteristic sensitivity in Ultrasound, with a weighted average of 4. They are least satisfied with objective quantification, which has a weighted average of 2.7. In comparison to MRI, duration of scan scores much better, with a weighted average of 3.9. Satisfaction is beneath 3.5 in Ultrasound for the characteristics visualization of (damaged) bone and cartilage,

subjective and objective quantification. Visualization of (damaged) bone and cartilage is the 4th important characteristics and therefore shortcomings could be a threat for the device.

With regard to the performance of X-ray, rheumatologists are overall less satisfied with how it performs on the different criteria. Only 7.4% are very satisfied, 32.3% satisfied, 29.6% are neither satisfied nor dissatisfied, 19.8% are dissatisfied and 10.8% are very dissatisfied with all cases. Rheumatologists are most satisfied with the characteristic duration of scan, with a weighted average of 4.2 and least satisfied with visualization of tendons and ligaments (weighted average 1.7). Even the characteristics perceived as most important to rheumatologists have only a weighted average of 3.3.

Rheumatologists are in 2.2% of all cases very satisfied with how a CT-scan performs on the different criteria. In 42.3% of all cases they are satisfied, and in 42.2% neither satisfied nor dissatisfied. 10% are dissatisfied and 2.2% very dissatisfied. Rheumatologists are most satisfied with the characteristic quality of the images, with a weighted average of 3.8. They are least satisfied with the characteristics objective quantification and visualization of blood vessels, with a weighted average of 2.7 each.

„Put hands and feet into a monitor and get a quantitative measurement of the number of joints and the state of the disease, all this in the investigation room of the doctor and nice visualized for the patient.“

This statement one of the rheumatologists made in the questionnaire sums up a lot about how rheumatologists perceive an ideal diagnostic tool for rheumatoid arthritis. Making the images in the investigation room is mentioned very often by rheumatologists. It would make a device immediately available if it is needed, the damage could be seen immediately, no referral would be needed and it would therefore make the whole diagnostic process faster. Another important issue is the ease of use of a device. Some rheumatologists state that a medical employee should be able to operate the device and interpret the results. For many of the rheumatologists it is important to see inflammation and erosion in a very early stage, and to investigate them in real time, like a “camera in the joint”. The costs of the devices were another often mentioned issue. The device should be cheaper than MRI. Besides that sensitivity and specificity were often mentioned characteristics. 7 rheumatologists mentioned that differentiation from other rheumatic diseases is an important feature of a device. Furthermore rheumatologists see objectivity of a device as an ideal characteristic, whereas there are also some who say that the best “device” is the rheumatologist himself and that an ideal tool “Is not available and will never be. Rheumatology is only as good as the specialist, independent from the tool”.

Most of the features an ideal diagnostic tool should have are also mentioned with regard to an ideal monitoring tool. The rheumatologists put more focus on the sensitivity and specificity of this device with regard to very small changes. Furthermore an automatic comparison with preliminary assessments was seen as an ideal feature.

According to the rheumatologists, different future developments in diagnosis and monitoring of rheumatoid arthritis are important. One can assume that imaging devices are going to play a major role in diagnosis and monitoring of rheumatoid arthritis. Small joint MRI and PET scan are seen as important developments by 7 respondents. Besides imaging technologies, the use of biomarkers is often mentioned. Furthermore the use of these devices in daily practice is an

important development the respondents identified. The devices should be easy to use and accessible when required. Besides this, there is a trend towards more education of patients and assistants.

The problems with sensitivity and specificity in diagnosis and monitoring are reflected in the answers on the questions which changes rheumatologists would desire. More sensitivity and specificity were mentioned about four times each. Besides this, especially faster measurement, earlier diagnosis, the ability to make a better prognosis and quantitative measurements as well as cheaper devices were desirable. Also less complexity in the usage and a tool that can be used by patients themselves for monitoring was mentioned. Some rheumatologists also want a tool that can locate erosions better. A database was also a central concept stated. Rheumatologists wish to have a database where they can compare different measurements and follow over time.

With regard to RAPACT, about 17% of rheumatologists (N= 35) rate the advantages the device can provide as very important and about 40% (N=35) regard them as important. Disadvantages of RAPACT were that the assessment of big joints is difficult and there are problems with the visualization of bone structure. These are both important characteristics for imaging devices according to the rheumatologists; therefore the disadvantages of RAPACT are even more important to rheumatologists. Asked about the arising of a future demand for this technology, more than a half of the rheumatologists state that a future demand might be probable, and 21% (N= 35)estimate this demand to be very probable.

The aim of this study was to perform a needs assessment in an early stage of the medical device development process of a new device for diagnosis and monitoring of rheumatoid arthritis.

During a needs assessment, information about opinions, attitudes and statements of individual groups is collected [84, 85]. This study focused on the group of medical device users. A medical device user is a person who uses a medical device for the treatment and/or care of him/or herself or someone else" [86]. According to this definition, different users can be identified: Patients, General Practitioner, Radiologists and Rheumatologists. These users are very heterogeneous and may have conflicting and/or different goals and wishes and there might be variations in needs and wishes according to age, ethnicity, experience, educational background, amount of type and training and (with regard to patients) the diagnostic process they went through. It was decided to focus this study on rheumatologists, as they are the health care professionals who make the definite diagnosis and are most likely the main users of the device presented in the case study.

In this study a self-administered questionnaire was executed for rheumatologist in the Netherlands, the United Kingdom and Germany. Through the self-administered questionnaire, information about the needs, wants and expectations of rheumatologists was gathered and met and unmet needs were identified. This approach is called health needs assessment. A health needs assessment (HNA) is an approach to understand the health and health care needs of a population to tailor health services [87]. Health care needs are those that can benefit from health care , such as the interventions that produce benefit for the population (health protection, prevention). They are met by the health care system [88]. Health needs is a broader concept. It included wider social and environmental determinants of health. It is met by the health care system and other social and economic initiatives [89].

At the moment, the imaging devices playing a role in diagnosis and monitoring of rheumatoid arthritis according to literature are MRI, Ultrasound, X-ray and CT-scan. X-ray is perceived as gold standard, but is more or less useless in early diagnosis. Ultrasound can assess synovitis, which is an indicator for rheumatoid arthritis, but changes in the bone are not easily to access. Furthermore the interpretation is quite complex. MRI is able to assess synovitis as well as changes in the bone. However, MRI is quite costly and not widely available and multiple joints cannot be assessed at the same time with the same quality. Despite the ability of CT-scans to perform examination of the hands and wrists in a very short time and its ability to provide clearer images than conventional X-ray, CT-scans are rarely used in clinical practice for diagnosis and monitoring of rheumatoid arthritis. Reasons for this that could be identified through literature study are that CT-scans use harmful radiation and have a low sensitivity to soft tissues changes in comparison with MRI and Ultrasound. Furthermore the interpretation of the images is complex. According to the changes in diagnosis and monitoring of rheumatoid arthritis that were identified during literature study, imaging devices are going to play a greater role in diagnosis and monitoring of rheumatoid arthritis. However, the SWOT analysis showed that at present there is no device that can display all features of (early) rheumatoid arthritis diagnosis. Every device has its advantages and disadvantages.

According to the questionnaire, sensitivity, specificity and quality of the images are the most important characteristics of imaging devices for diagnosis and monitoring of rheumatoid arthritis. Visualization of blood vessels is perceived as least important characteristic by the rheumatologists.

When comparing the importance of the different characteristics with the performance (satisfaction) of the devices, it becomes apparent that there are differences in between how

important a characteristic is and how well it performs. Even though sensitivity is the most important characteristic, X-ray and CT-scan have values/weighted averages below 4 (satisfied). For specificity, all weighted averages are below 4, but all of them except X-ray are close to 4. Assessment of big joints is the characteristic rheumatologists are overall most satisfied with, but it is not considered that important (rank 6th). The characteristics visualization of blood vessels and objective assessment score in none of the devices a 4 and rarely a 3, but they are also the least important characteristics. However, recent studies suggest that the development of small blood vessels in the synovium is one of the earliest signs of rheumatoid arthritis. The qualitative data analysis of the questionnaire identifies a trend to more objective measurements. When this trend continues and rheumatologists get more aware of the importance of blood vessels in rheumatoid arthritis, importance of these characteristics might increase, and action should be taken by decision makers to fulfill the increased demand.

Rheumatologists indicated in the qualitative part of the questionnaire, that they have problems with sensitivity and specificity of current devices. Surprisingly, when asked about the satisfaction of these characteristics in different imaging devices, rheumatologists only rated the performance of X-ray and CT as not satisfying (weighted average below 4). None of the rheumatologists rated MRI or Ultrasound to be very dissatisfying or dissatisfying. However, in Ultrasound about 18% rated sensitivity and about 39% specificity to be neither satisfied nor dissatisfied with, and in MRI this was 16% and 37% respectively. This result is an indication that rheumatologists are not satisfied with these characteristics, because they choose the neutral option "neither satisfied nor dissatisfied". Removal of the neutral option might have led to more rheumatologists rating the performance of the devices as dissatisfying. When comparing the results of the literature study with the findings of the questionnaire, some discrepancies in the findings could be observed. According to the SWOT analysis, the assessment of the bone structure is very difficult with Ultrasound; however, rheumatologist did not indicate dissatisfaction with this characteristic. This might be due to the fact that Ultrasound cannot penetrate bone but studies have shown the ability of Ultrasound to detect bone abnormalities and cartilage [90-92]. Literature indicates shortcomings in image quality in MRI, ultrasound, X-ray and CT-scan. This study could not acknowledge these findings, as rheumatologists rated image quality in all devices above a weighted average of 3.5.

Rheumatologists mentioned X-ray and Ultrasound the most when asked about problems they have with devices. This can be explained by the fact that these are also the imaging devices used the most. The quantitative analysis supports the statements of the rheumatologists with regard to X-ray, as 7 out of 10 criteria are rated with a weighted average below 3.5. The usage of these devices despite the shortcomings they have might be an indication for the fact that there is no other adequate imaging technology.

An imaging technology that could fill this gap and address future needs is RAPACT. 53% of rheumatologists' state that a future demand for RAPACT in their practice is very probable and about 53% state that a future demand is probable. 26% think that there is probably no future demand for RAPACT in their practice. A study by Kent [93] indicated that respondents assign a probability of 63 – 87% to the word probable, which means that overall, rheumatologists are positive about a future demand for RAPACT.

With regard of the likelihood of additional value RAPACT might have, there is no clear picture. About 23% tend toward a larger likelihood and 37% towards a smaller likelihood. 34% choose the middle option. The small tendency towards a smaller likelihood might be explained by the fact that the disadvantages of RAPACT are perceived as even more important than its advantages. Visualization of (damaged) bone and cartilage scored 4th important amongst rheumatologists. If there are improvements in these areas, the additional value of RAPACT will very probably increase.

The potential of RAPACT is difficult to access, as many things are still uncertain, and it is not known how RAPACT would score on the different characteristics. Furthermore, the trend towards early diagnosis might have a great influence on the relative advantage RAPACT might have over other devices. At the moment, rheumatologists are quite satisfied with how X-ray displays erosion and cartilage. However, this visualization is only possible in later stages of the disease. With more urge for earlier diagnosis, rheumatologists might get less satisfied with the abilities of this device. MRI is still too costly and not widely available. New forms of MRI are a potential threat to RAPACT.

RAPACT could lead to cost savings in rheumatoid arthritis, if it can detect rheumatoid arthritis earlier and monitor disease progression better than other devices, which could lead to a more tailored treatment approach. Developers expect the costs of RAPACT to be lower than MRI. If the device is less costly than MRI, substitution might lead to major cost savings, as a study of Parker & Nazarian[94] revealed. In the study the substitution of MRI with Ultrasound led to cost savings of several billion dollars.

The device that was evaluated in this study is at a relatively early stage of the medical device development process. The involvement of users in an early phase of medical product development could result in products that improve patient safety, device effectiveness and reduce the need for (costly) product recalls and modifications [95, 96]. However, there are certain problems when conducting user involvement studies. Many developers of a medical device do not consider the needs of the users because they do not see the necessity to do so. If developers see the necessity to involve users, they might not know how to incorporate the needs of the user in the development process and/or do not have the time and resources to involve them [97, 98]. This research underpinned that developers are focused on the technical side of the device and do not consider other important aspects like user needs. The developers of the device that served as case in this study did not consider incorporating user needs during the (early) stages of the development process.

Because of the early stage of the medical device development process of the device, the developers are still working on the technical aspects of the device. Contact with the developers was held during the execution of this project to gather additional information about technical details of the device, inform the developers about the progress of the project and verify the information of the device that was given in the questionnaire.

There is a lot of uncertainty about the value the device can have in diagnosis and monitoring of rheumatoid arthritis in this early stage of development. Rheumatologists needed to make judgments about the device based on information that was conducted by the researcher through information the developers provided and the project proposal of the company. It was expected most of the respondents did not know the device under assessment. Therefore a short introductory paragraph about the device was given which was the same for all respondents. There is therefore a certain risk that respondents might not understand some aspects of the device and because of the chosen method of this research they could not ask additional questions during the execution of the questionnaire. It might therefore been difficult for the users to make a judgment about the new device.

The opinions of the rheumatologists should be seen as a snap-shot. More information and validated measurements of RAPACT would lead to more explicit estimations of the added value of RAPACT. If characteristics like sensitivity and specificity of the device are known, better comparisons with other imaging devices and more specific estimations about the place of the device in the care pathway of rheumatoid arthritis can be made. Information gained through this study gives insights into the characteristics that are important for rheumatologists. This information can be used by the developers to adjust their device so that it meets these requirements and it shows upcoming needs the device might fulfill. As more data are available,

more research can be made. As soon as more details about RAPACT are known with regard to its performance, rheumatologists can make estimations about these values with regard to different characteristics. Rheumatologists scored devices relatively well but in the qualitative part they state to have problems. To explore this discrepancy would be interesting.

STRENGHTS AND LIMITATIONS

The first strength of this research is that it involves users early in the development process of a new medical device, which could result in a device that truly meets the requirements of its users [99]. Another strength is that quantitative and qualitative data were collected and analysed. "Different but complementary data on the same topic" can be gathered, leading to a better understanding of the data than using either dataset alone [17, 100].

The usage of a self-administered questionnaire has several advantages. First of all it is less time consuming than interviews, and a lot of people that are geographically distributed can be reached at the same time, which was of great interest for this research that was performed among rheumatologists of the United Kingdom, Germany and the Netherlands. Furthermore the anonymity of the respondents can lead to more valid responses and there are no interviewer biases. Besides that the costs of self-administered questionnaires are lower than telephone or face to face interviews [101].

One of the main limitations of self-administered questionnaires is that the response rate might be low. The number of rheumatologists that took part in the questionnaire was limited. In total 38 rheumatologists executed the survey. One respondent was excluded from the analysis because only three questions were answered. Two respondents were excluded because they took less than two minutes to answer the survey, which was estimated as not enough time to read all questions carefully and provide answers. In the Netherlands 71 rheumatologists were asked to participate. From these 71 rheumatologists, 25 participated in the survey, which is a response rate of 35%. A response rate of 50% is regarded as adequate [19]. The calculation of the response rates is only available for the Netherlands, because the participants of other countries were mostly reached through the Intranet of organizations, what makes it impossible to calculate how many people actually took part in the questionnaire. Rheumatologists in the Netherlands were only reached through e-mails. Another problem is that not all important characteristics for diagnosis and monitoring have been analyzed, as this would have made the questionnaire too complex. Characteristics were chosen on basis of literature and after consideration with a rheumatologist during the pilot testing of the questionnaire. For this reason the overall picture of the rheumatologists' needs assessment might not be complete. Another limitation is that the respondents might have been influenced by the quantitative part of the survey when answering the qualitative part. There might have been an overestimation of the own ability of the rheumatologists, leading to neglecting of problems such as a lack of adequate devices for diagnosis of rheumatoid arthritis. This can be a major problem, as a wrong diagnosis based on clinical findings can delay effective treatment of rheumatoid arthritis.

Other methods that might be useful in future research are Analytic Hierarchy Process (AHP) and conjoint analysis. In this study these methods have been abandoned, since the conversion of verbal to numerical data as done with AHP does not always reflect the preference of the decision maker and conjoint analysis gives no detailed insights and with a growing number of attributes, restrictions in the design have to been made [102-105].

It might be interesting to examine in how far the results of this research really contribute to the development of the medical device, which could give more insights into the process of user involvement and the performance of (early) HTA.

This research made clear that the involvement of end users in the needs assessment study can be very difficult for two reasons. The first is the limited time they have and the second is that organizations/associations refused to collaborate, which might be an indication for the underestimation of this topic.

CONCLUSION

The role of imaging devices in diagnosis and monitoring of rheumatoid arthritis is expanding and imaging devices are getting increasingly integrated into recommendations and guidelines for rheumatoid arthritis.

The results from the needs assessment showed that there is a need for improvement in imaging devices used for diagnosis and monitoring of rheumatoid arthritis, as a majority of the rheumatologist state that there is a need for higher quality tools and a third of them have problems with the devices they are using.

Rheumatologists scored sensitivity, specificity, quality of the images and visualization of (damaged) bone and cartilage as most important criteria. Visualization of blood vessels, duration of the scan and objective quantification are the least important criteria.

Overall, rheumatologists were least satisfied with the performance of all devices with regard to objective quantification, followed by the visualization of blood vessels. Rheumatologists were most satisfied with the performance of all devices with regard to the assessment of big joints, followed by quality of the images.

With regard to the open ended questions there seems to be a trend towards less complex devices that can be used in daily practice. At the moment, none of the devices on the market are able to fulfill this need, but as imaging devices like MRI are getting more modified and other competitors (e.g. handscan) are entering the market, this niche is going to be highly competitive [106].

RAPACT has chances to implementation in daily practice if the device is less costly than MRI and easy to use in daily practice. A combination with Power Doppler Ultrasound might be favorable for the adoption process, as Ultrasound is already available in many practices and the fusion of data might result in a device with great competitive advantage. With early detection of rheumatoid arthritis getting more important and characteristics like visualization of blood vessels and objective measurements getting more attention, the additional value of RAPACT might increase and the possibility to use RAPACT as a monitoring tool would get more attractive to rheumatologists. If RAPACT shows possibility as a tool for differential diagnosis, this might increase its value for diagnostic purposes.

However, proof of principle of RAPACT is still needed and (other) devices are constantly improving. Furthermore the disadvantages of RAPACT are perceived as important to rheumatologists, what makes adaption difficult.

Studies showing the importance of blood flow in rheumatoid arthritis and usage of modified imaging devices like diffusion- weighted MRI and multi-modal technologies like PET/CT were mentioned as important developments by rheumatologists in this study and might indicate a trend towards more functional imaging, which is in line with findings of other studies [107, 108].

The possibility of RAPACT as a multi-modal imaging technology with the ability to provide anatomic and functional data is promising, but further research is needed to verify the results and get more information about the attitude of rheumatologists towards this specific technology.

REFERENCES

1. PricewaterhouseCoopers, *The Factors Fueling Rising Healthcare Costs*, 2002: Washington DC.
2. Calman, K.C., *The ethics of allocation of scarce health care resources: a view from the centre.* Journal of Medical Ethics, 1994. **20**(2): p. 71-74.
3. Grimes, D.A., *Technology Follies. The Uncritical Acceptance of Medical Innovation.* The Journal of the American Medical Association, 1993. **269**(23): p. 3030-3033.
4. Committee on Technology and Health Care, et al., *Medical Technology and the Health Care System. A Study of the Diffusion of Equipment-Emodied Technology*, 1979: Washington D.C.
5. International Network of Agencies for Health Technology Assessment. *INAHTA Health Technology Assessment (HTA) Glossary*. 2006 [cited 2013 02.06.2013]; Available from: http://www.inahta.org/Glossary/#_G.
6. Berrettini, S., et al., *Analysis of the impact of professional involvement in evidence generation for the HTA Process, subproject "Cochlaer Implants" : methodology, results and recommendations.* Acto Otorhinolaryngologica italica, 2011: p. 273-280.
7. Health Equality Europe, *Understanding Health Technology Assessment (HTA).* 2008.
8. n.a., *Photoacoustic Imaging and Spectroscopy*. 2009: CRC Press Taylor & Francis Group.
9. Banta, H.D. and B.R. Luce, *Health Care Technology and Its Assessment: An International Perspective*. Oxford Medical Publications. 1993: Oxford University Press. 384.
10. Habbema, J.D.F., et al., *Medische Technology Assessment en gezondheidsbeleid*. 1989, Alphen aan den Rijn: Samson Stafleu.
11. IJzerman, M.J. and L.M.G. Steuten, *Early Assessment of Medical Technologies to Inform Product Development and Market Access. A Review of Methods and Applications.* Applied Health Economics and Health Policy, 2011: p. 1-17.
12. Dorsey, E.R., et al., *Funding of US Biomedical Research, 2003-2008.* The Journal of the Americam Medical Association, 2010. **303**(2): p. 137-143.
13. University of Twente. *Health Technology Assessment*. n.d. [cited 2013; Available from: http://www.google.de/imgres?start=90&um=1&client=firefox-a&sa=N&rls=org.mozilla:de:official&hl=en&biw=1600&bih=796&tbm=isch&tbnid=SCZ359xD5rIEMM:&imgrefurl=http://www.utwente.nl/mb/htsr/Valorisation/Where%2520technology%2520meets%2520healthcare/&docid=CYNWjaQcNITOlM&imgurl=http://www.utwente.nl/mb/htsr/Valorisation/Where%252520technology%252520meets%252520healthcare/Where%252520technology%252520meets%252520healthcare-1.png&w=530&h=395&ei=NiMSUvyYGIiatQbvy4HYBg&zoom=1&iact=hc&vpx=1046&vpy=473&dur=263&hovh=194&hovw=260&tx=97&ty=61&page=3&tbnh=158&tbnw=212&ndsp=56&ved=1t:429,r:6,s:100,i:22.
14. van de Wetering, G., et al., *Early Bayesian modeling of a potassium lab-on-a-chip for monitoring of heart failure patients at increased risk of hyperkalaemia.* Technological Forecasting & Social Change, 2012: p. 1268-1279.
15. Pietzsch, J.B. and M.E. Pate-Cornell, *Early technology assessment of new medical devices.* International Journal of Technology Assessment in Health Care, 2008. **24**(1): p. 36-44.
16. van Es, P., *Different areas of study*, 2013.
17. Creswell, J.W. and V.L. Plano Clark, *Designing and Conducting Mixed Methods Research*. 2007, Thousand Oaks, California: Sage Publications.
18. Strauss, A. and J. Corbin, *Basics of Qualitative Research: Techniques and Procedures for Developing Grounded Theory*. 1998, Thousand Oaks: Sage Publications Inc.
19. Babbie, E., *The Practice of Social Research*. 11 ed. 2007: Thomson Wadsworth.
20. National Institute of Arthritis and Musculoskeletal and Skin Disease, *Handout on Health: Rheumatoid Arthritis*, 2009.
21. Medline Plus, *Rheumatoid Arthritis*, 2013.

22. National Collaborating Centre for Chronic Conditions, *Rheumatoid arthritis: national clinical guideline for management and treatment in adults*, 2009, Royal College of Physicians: London.
23. Arthritis Foundation, *Rheumatoid Arthritis*, n.d.
24. Panayi, G., *What is RA*, 2011.
25. National Health Service, *Causes of rheumatoid arthritis*, 2012.
26. Sommer, O.J., et al., *Rheumatoid Arthritis: A Practical Guide to State-of-the-Art Imaging, Image Interpretation, and Clinical Implications*, in *RadioGraphics*2005. p. 381-398.
27. Strand, V., R. Kimberly, and J.D. Isaacs, *Biologic therapies in rheumatology: lessons learned, future directions.* Nat Rev Drug Discov, 2007. **6**(1): p. 75-92.
28. National Institute for Health and Care Excellence. *NICE Pathways*. Rheumatoid arthritis overview 2013 [cited 2013; Available from: http://pathways.nice.org.uk/pathways/rheumatoid-arthritis.
29. Schäfer, W., et al., *Health Systems in Transition*, in *The Netherlands: Health system review*, E. Mossialos, Editor 2010.
30. The Commonwealth Fund, *International Profiles of Health Care Systems* 2012.
31. Temprano, K.K., *Medscape Reference*, 2013.
32. Nederlandse Vereniging voor Reumatologie, *Diagnostiek en behandeling van reumatoïde artritis*. 2009, Utrecht: Van Zuiden Communications B.V.
33. Schneider, M., et al., *Interdisziplinäre Leitlinie*, in *Management der frühen rheumatoiden Arthritis*2011, Springer Verlag GmbH: Berlin.
34. Combe, B., et al., *EULAR recommendations for the management of early arthritis: report of a task force of the European Standing Committee for International Clinical STudies Including Therapeutics (ESCISIT).* Annals of the Rheumatic Diseases 2007. **66**: p. 34-45.
35. Emery, P. and P. Symmons, *What is early rheumatoid arthritis? Definition and diagnosis.* Bailliere's clinical rheumatology, 1997: p. 13-26.
36. Suresh, E., *Diagnosis of early rheumatoid arthritis: what the non-specialist needs to know.* Journal of the Royal Society of Medicine, 2004: p. 421-424.
37. Egsmose, C., et al., *Patients with rheumatoid arthritis benefit from early 2nd line therapy: 5 year followup of a prospective double blind placebo controlled study.* Journal of Rheumatology, 1995: p. 2208-2213.
38. Symmons, D., et al., *Longterm mortality outcome in patients with rheumatoid arthritis: early presenters continue to do well.* Journal of Rheumatology, 1998: p. 1072-1077.
39. Anderson, J.J., et al., *Factors predicting response to treatment in rheumatoid arthritis: the importance of disease duration.* Arthritis & Rheumatism, 2000: p. 22-29.
40. Puolakka, K., et al., *Impact of initial aggressive drug treatment with a combination of disease-modifying antirheumatic drugs on the development of work disability in early rheumatoid arthritis: a five-year randomized followup trial.* Arthritis & Rheumatism, 2004. **50**(1): p. 55-62.
41. Finckh, A., et al., *Long-temr impact of early treatment on radiographic progression in rheumatoid arthritis: A meta-analysis.* Arthritis & Rheumatism, 2006. **55**(6): p. 864-872.
42. Deutscher Bundestag, *Maßnahmen zur Verbesserung der Versorung von Patienten mit entzündlich - rheumatischen Erkrankungen*, 2011: Berlin.
43. Schepman, S.M., R.S. Batenburg, and J. hansen, *De arbeidsmarkt voor reumatologen in Nederland*, in *genoeg reumatologen om reumapatiënten in beweging te houden?*2010, Netherlands institute for health services research , : Utrecht.
44. Westhoff, G., et al., *Advance and unmet need of health care for patients with rheumatoid arthrtis in the German population - results from the German Rheumatoid Arthritis Population Survey (GRAPS).* Rheumatology, 2009. **48**: p. 650-657.
45. Pease, C., et al., *Comparison of anti - TNF treatment initiation in rheumatoid arthritis databases demnostrates wide country variability in patient parameters at initiation of anti - TNF therapy.* Seminars in arthritis and rheumatism, 2011. **41**(1): p. 81-89.
46. Chan, K., et al., *The lag time between onset of symptoms and diagnosis of rheumatoid arthritis.* Arthritis & Rheumatism, 1994. **37**(6): p. 814-820.

47. Raza, K., et al., *Delays in assessment of patients with rheumatoid arthritis: variations across Europe.* Annals of the Rheumatic Diseases, 2011. **70**: p. 1822-1825.
48. Garneau, K., et al., *Primary care physicians' perspectives towards managing rheumatoid arthritis: room for improvement.* Arthritis Research & Therapy, 2011. **13**(6): p. R189.
49. Suter, L.G., L. Fraenkel, and E.S. Holmboe, *What factors account for referral delays for patients with suspected rheumatoid arthritis?* Arthritis & Rheumatism, 2006. **55**(2): p. 300-305.
50. Bolumar, F., et al., *Reliability of the diagnosis of rheumatic conditions at the primary health care level.* Journal of Rheumatology, 1994. **21**(12): p. 2344-2348.
51. Gamez-Nava, J.I., et al., *Referral and diagnosis of common rheumatic diseases by primary care physicians.* British journal of rheumatology, 1998. **37**(11): p. 1215-1219.
52. Aletaha, D., et al., *Atitudes to early rheumatoid arthritis: changing patterns. Results of a survey.* Annals of the Rheumatic Diseases, 2004. **63**(10): p. 1269-1275.
53. Rat, A.C., V. Henegariu, and M.C. Boissier, *Do primary care physicians have a place in the management of rheumatoid arthritis?* Joint Bone Spine, 2004. **71**(3): p. 190-197.
54. Aletaha, D., et al., *Practical progress in realisation of early diagnosis and treatment of patients with suspected rheumatoid arthritis: results from two matched questionnaires within three years.* Annals of the Rheumatic Diseases, 2002. **61**(7): p. 630-640.
55. Green, M., et al., *Persistence of mild, early inflammatory arthritis: the importance of disease duration, rheumatoid factor, and the shared epitope* Arthritis and rheumatism, 1999. **42**(10): p. 2184-2188.
56. Symmons, D. and B. Harrison, *Early inflammatory polyarthritis: results from the Norfolk Arthritis Register with a review of the literature. I. Risk factors for the development of inflammatory polyarthritis and rheumatoid arthritis.* Rheumatology, 2000. **39**(8): p. 835-843.
57. Zink, A., et al., *National database of German arthritis centers. Tool for health services research.* Bundesgesundheitsblatt Gesundheitsforschung Gesundheitsschutz, 2004. **47**(6): p. 526-532.
58. Colebatch, A.N., et al., *EULAR recommendations for the use of imaging of the joints in the clinical management of rheumatoid arthritis.* Annals of the Rheumatic Diseases, 2013.
59. Peterfy, C.G., T. Roberts, and H.K. Genant, *Dedciated extremity MR imaging: An emerging technology.* Magnetic resonance imaging clinics of North America, 1998. **6**(4): p. 849-870.
60. Ejbjerg, B.J., et al., *Optimised, low cost, low field dedicated extremity MRI is highly specific and sensitive for synovitis and bone erosions in rheumatoid arthritis wrist and finger joints: comparison with conventional highfield MRI and radiography.* Annals of the Rheumatic Diseases, 2005. **64**(9): p. 1280-1287.
61. Freeston, J.E., P. Bird, and P.G. Conaghan, *The role of MRI in rheumatoid arthritis: research and clinical issues.* Current Opinion in Rheumatology, 2009. **21**(2): p. 95-101.
62. Miese, F.R., et al., *Metacarpophalangeal Joints in Rheumatoid Arthritis: Delayed Gadolinium - enhanced MR Imaging of Cartilage - A Feasibility Study.* Radiology, 2010. **269**(1): p. 441-447.
63. Neubauer, H., et al., *Diffusion - weighted MRI of bone marrow oedema, soft tissue oedema and synovitis in paediatric patients: feasibility and initial experience.* Pediatric Rheumatology Online Journal, 2012. **10**(1).
64. Jeromel, M., et al., *Quantification of synovitis in the cranio - cervical region: dynamic contrast enhanced and diffusion weighted magnetic resonance imaging in early rheumatoid arthrits - a feasibility follow up study.* European journal of radiology, 2012. **81**(11): p. 3412-3419.
65. Backhaus, M., et al., *Prospective two year follow up study comparing novel and conventional imaging procedures in patients with arthritic finger joints.* Annals of the Rheumatic Diseases, 2002. **61**(10): p. 895-904.
66. Boesen, M., et al., *MRI quantification of rheumatoid arthritis: Current knowledge and future perspectives.* European Journal of Radiology, 2009. **71**: p. 189-196.

67. Mandl, P., et al., *A systematic literature review analysis of ultrasound joint count and scoring systems to assess synovitis in rheumatoid arthritis according to the OMERACT filter.* The Journal of rheumatology, 2011. **38**(9): p. 2055-2062.
68. Wells, A.F. and R.H. Haddad, *Emerging role of ultrasonography in rheumatoid arthritis: optimizing diagnosis, measuring disease activity and identifying prognostic factors.* Ultrasound in medicine & biology, 2011. **37**(8): p. 1173-1184.
69. Chen, Y.-C., T.-T. Cheng, and S.-W. Hsu, *Ultrasound in rheumatoid arthritis.* Formosan Journal of Rheumatology, 2009. **23**: p. 1-7.
70. Cairns, A. and A. Taggart. *Imaging techniques in rheumatology* 2004 15.11.2011; Available from: http://nras.org.uk/about_rheumatoid_arthritis/what_is_ra/how_is_it_diagnosed/imaging_techniques_in_rheumatology.aspx?mode=print.
71. Cimmino, M.A., et al., *Imaging in arthritis: quantifying effects of therapeutic intervention using MRI and molecular imaging* Swiss Medical Weekly. The European Journal of Medical Sciences, 2012.
72. Bankhead, C. *Technology offers promises of newer, faster applications and challenges of data management*. 2002; Available from: http://www.diagnosticimaging.com/dimag/legacy/advancedCT2002/4.html.
73. West, A.T.H., T.J. Marshall, and P.W. Bearcroft, *CT of the musculoskeletal system: What is left is the days of MRI?* European journal of radiology, 2009. **19**: p. 152-164.
74. European Commission, *Exploratory Proces on the Future of the Medical Devices*, in *Potential themes for further reflection at the European level and Issues identified by the Members*2010, European Commission,: Brussels.
75. Aletaha, D., et al., *2010 Rheumatoid Arthritis Classification Criteria.* Arthritis & Rheumatism, 2010. **62**(9): p. 2569-2581.
76. Peterfy, C.G., *New developments in imaging in rheumatoid arthritis.* Current Opinion in Rheumatology, 2003: p. 288-295.
77. Irvine, S., R. Munro, and D. Porter, *Early referral, diagnosis, and treatment of rheumatoid arthritis: evidence for changing medical practice.* Annals of the Rheumatic Diseases, 1999. **58**(8): p. 510-513.
78. Cush, J.J., *Early Arthritis Clinics: If you Build It Will They Come?* The Journal of rheumatology, 2005. **32**(2): p. 203-207.
79. van der Linden, M.P., et al., *Long - term impact of delay in assessment of patients with early arthritis.* Arthritis & Rheumatism, 2010. **62**(12): p. 3537-3546.
80. Goekoop-Ruiterman, Y.P., et al., *Comparison of treatment strategies in early rheumatoid arthritis: a randomized trial.* Annals of internal medicine, 2007. **146**(6): p. 406-415.
81. Grigor, C., et al., *Effect of a treatment strategy of tight control for rheumatoid arthritis (the TICORA study): a single-blind randomised controlled trial.* Lancet, 2004. **364**(9430): p. 263-269.
82. Smolen, J.S., et al., *Treating rheumatoid arthritis to target: recommendations of an international task force.* Annals of the Rheumatic Diseases, 2010. **69**: p. 631-637.
83. Peterfy, C.G., *MRI of thw wrist in early rheumatoid arthritis.* Annals of the Rheumatic Diseases, 2004. **63**: p. 473-477.
84. Jacobsen, M.J., A.M. O'Connor, and D. Stacey, *Decisional Needs Assessment in Populations*, in *A workbook for assessing patients' and practitioners'decision making needs*1999.
85. Bridges, J.F.P., et al., *Priorities for Hepatocellular Carcinoma (HCC) Control: A Comparison of Policy Needs in Five European Countries.* Journal of Comparative Policy Analysis: Research and Practice, 2012. **14**(4): p. 352-368.
86. Shah, S.G.S. and I. Robinson, *Medical device technologies: who is the user?* International Journal of Healthcare Technology and Management, 2008: p. 181-197.
87. Stevens, A. and S. Gillam, *Needs assessment: from theory to practice.* British Medical Journal, 1998. **316**(7142): p. 1448-1452.
88. Stevens, A., et al., *Health Care Needs Assessment. The epidemiologically based needs assessment reviews*. 2004, United Kingdom: Radcliffe Publishing Ltd.

89. Ardal, S., et al., *Assessing Need.* , in *The Health Planner's Toolkit*2006, Health System Intelligence Project. p. 1-50.
90. Wakefield, R. and M.-A. D'Agostino, *Essential Applications of Musculoskeletal Ultrasound in Rheumatology*. 2010, Philadelphia: Saunders.
91. Grassi, W., et al., *Ultrasound examination of metacarpophalangeal joints in rheumatoid arthritis.* Scandinavian Journal of Rheumatology, 1993. **22**(5): p. 243-247.
92. Grassi, W., et al., *Sonographic imaging of normal and osteoarthritic cartilage.* Seminars in Arthritis and Rheumatism, 1999. **28**(6): p. 398-403.
93. Kent, S. *Words of Estimative Probability*. 1964 07.07.2008 [cited 2013; Available from: https://www.cia.gov/library/center-for-the-study-of-intelligence/csi-publications/books-and-monographs/sherman-kent-and-the-board-of-national-estimates-collected-essays/6words.html.
94. Parker, L., et al., *Musculoskeletal imaging: medicare use, costs and potential for cost substitution.* Journal of the American College of Rheumatology, 2008. **5**(3): p. 182-188.
95. Martin, J.L., et al., *Capturing user requirements in medical device development: the role of ergonomics.* Physiological Measurement, 2006: p. 49-62.
96. De Vito Dabbs, A., et al., *User-Centered Design and Interactive Health Technologies for Patients.* Computers, Informatics, Nursing, 2009. **27**(3).
97. Kujala, S., *User involvement: a review of the benefits and challenges.* Behaviour and Information technology, 2003: p. 1-16.
98. Shah, S.G.S. and I. Robinson, *Benefits and barriers to involving users in medical device technology development and evaluation.* International Journal of technology Assessment in Health Care, 2007: p. 131-137.
99. Martin, J.L., M.P. Craven, and B.J. Norris, *MATCH: A new industry-focused approach to medical device development*, in *Proceedings on the International Conference on Healthcare Systems Ergonomics and Patient Safety*2005.
100. Creswell, J.W., et al., *Advanced mixed methods research designs*, in *Handbook of mixed methods in social and behavioral research*, A. Tashakkori and C. Teddlie, Editors. 2003, Sage Publications: Thousand Oaks, California. p. 209-240.
101. n.a., *The SAGE Encyclopedia of social science research methods*, ed. M.S. Lewis - Beck, A. Bryman, and T. Futing Liao. Vol. 1. 2004, Thousand Oaks, California: Sage Publications.
102. Hummel, M., et al., *Applying the AHP in health economic evaluations of new technology*, in *Proceedings of the International Symposium on the Analytic Hierachy Process* 2011: Sorrento.
103. Goodwin, P. and G. Wright, *Decision Analysis for Management Judgment*. 2009, Chichester: John Wiley & Sons. 468.
104. Dodgson, J., et al., *DTLR multi - criteria analysis manual*, 2001.
105. Belton, V. and P. Goodwin, *Remarks on the application of the analytic hierarchy process to judgmental forecasting.* International Journal of Forecasting, 1996. **12**(1): p. 155-161.
106. Hemics BV. *Technology Basics*. 2013; Available from: http://www.hemics.com/technology.
107. Zeman, M.N. and P.J.H. Scott, *Current imaging strategies in rheumatoid arthritis.* American Journal of Nuclear Medicine and Molecular Imaging, 2012. **2**(2): p. 174-220.
108. Kubota, K., et al., *FDG PET for rheumatoid arthritis: basic considerations and whole - body PET/CT.* Annals of the New York Academy of Science, 2011: p. 29-38.
109. van Gestel, A.M., et al., *Development and validation of the European League Against Rheumatism response criteria for rheumatoid arthritis.* Arthritis & Rheumatism, 1996. **39**(1).
110. Pinals, R.S., et al., *Preliminary criteria for clinical remission in rheumatoid arthritis.* Arthritis & Rheumatism, 1981. **24**(10).
111. Stanford University, *ARAMIS: HAQ*, 2003.
112. Stucki, G., et al., *A self-administered rheumatoid arthritis disease activity index (RADAI) for epidemiologic research.* Arthritis & Rheumatism, 1995. **38**(6): p. 795-798.

113. Kiely, P. *The DAS28 score*. 2011 28.03.2011; Available from: http://www.nras.org.uk/about_rheumatoid_arthritis/established_disease/managing_well/the_das28_score.aspx.
114. National Rheumatoid Arthritis Society, *DAS28. Quick reference guide*, 2010.
115. Schmitt, R. and U. Lanz, *Bildgebende Diagnostik der Hand*. 2004, Stuttgart: Georg Thieme Verlag.
116. van der Heijde, D., *How to read radiogrpahs according to the Sharp/van der Heijde method.* The Journal of rheumatology, 2000. **27**(1): p. 261-263.
117. Wolfe, F., et al., *Preliminary Core Set of Domains and Reporting Requirements for Longitudinal Observational Studies in Rheumatology.* The Journal of rheumatology, 1999. **26**(2): p. 484-489.
118. Smolen, J.S., et al., *A simplified disease activity index for rheumatoid arthritis for use in clinical practice.* Rheumatology, 2003. **42**: p. 244-257.
119. American College of Rheumatology, *SDAI Form*, n.d.
120. American College of Rheumatology, *CDAI Form*, n.d.
121. Østergaard, M., et al., *An introduction to the EULAR - OMERACT rheumatoid arthritis MRI reference image atlas.* Annals of the Rheumatic Diseases, 2005. **64**: p. i3-i7.
122. Combe, B., et al., *EULAR recommendations for the management of early arthritis: report of a task force of the European Standing Committee for International Clinical Studies Including Therapeutics (ESCISIT).* Annals of the Rheumatic Diseases, 2007. **66**(1): p. 34-45.
123. Østergaard, M., S.J. Pedersen, and U. Møller Døhn, *Imaging in rheumatoid arthritis - status and recent advantages for magnetic resonance imaging, ultrasonography, computed tomograhy and conventional radiography.* Best Practice & Research Clinical Rheumatology, 2008. **22**(6): p. 1019-1044.
124. Backhaus, M., et al., *Arthritis of the finger joints. A comprehensive approach comparing conventional radiography, scintigraphy, ultrasound and contrast - enhanced mangentic resonance imaging.* Arthritis & Rheumatism, 1999. **42**(6): p. 1232-1245.
125. Klarlund, M., et al., *Magnetic resonance imaging, radiography, and scintigraphy of the finger joints: one year follow up of patients with early arthritis.* Annals of the Rheumatic Diseases, 2000. **59**: p. 521-528.
126. Kosta, P.E., et al., *The usefulness of magnetic resonance imaging of the hand and wrist in very early rheumatoid arthritis.* Arthritis Research & Therapy, 2011. **13**(84).
127. McQueen, F.M., et al., *Magnetic resonance imaging of the wrist in early rheumatoid arthritis reveals progression of erosions despite clinical improvement.* Annals of the Rheumatic Diseases, 1999. **58**: p. 156-163.
128. Scheel, A.K., et al., *Prospective 7 year follow up imaging study comparing radiography, ultrasonography, and magnetic resonance imaging in rheumatoid arthritis finger joints.* Annals of the Rheumatic Diseases, 2006. **65**(5): p. 595-600.
129. Boutry, N., et al., *Early Rheumatoid Arthritis: A Review of MRI and Sonographic Findings* in *American Journal of Roentgenology*2007. p. 1502-1509.
130. Tan, Y.K., M. Østergaard, and P.G. Conaghan, *Imaging tools in rheumatoid arthritis: ultrasound vs magnetic resonance imaging* Rheumatology, 2012. **51**(7): p. 736-742.
131. McQueen, F.M., et al., *Magnetic resonance imaging of the wrist in early rheumatoid arthritis reveals a high prevalence of erosions at four months after symptom onset.* Annals of the Rheumatic Diseases, 1998. **57**(6): p. 350-356.
132. Brower, A.C., *Use of the radiograph to measure the course of rheumatoid arthritis: the gold standard versus fool's gold.* Arthritis & Rheumatism, 1990. **33**(3): p. 316-324.
133. World Health Organization, *Medical device regulations: Global overview and guiging principles*, 2003.

APPENDIX

APPENDIX A

ACR CRITERIA

	Score
Target population (Who should be tested?): Patients who	
1) have at least 1 joint with definite clinical synovitis (swelling)*	
2) with the synovitis not better explained by another disease†	
Classification criteria for RA (score-based algorithm: add score of categories A–D; a score of ≥6/10 is needed for classification of a patient as having definite RA)‡	
A. Joint involvement§	
1 large joint¶	0
2–10 large joints	1
1–3 small joints (with or without involvement of large joints)#	2
4–10 small joints (with or without involvement of large joints)	3
>10 joints (at least 1 small joint)**	5
B. Serology (at least 1 test result is needed for classification)††	
Negative RF *and* negative ACPA	0
Low-positive RF *or* low-positive ACPA	2
High-positive RF *or* high-positive ACPA	3
C. Acute-phase reactants (at least 1 test result is needed for classification)‡‡	
Normal CRP *and* normal ESR	0
Abnormal CRP *or* abnormal ESR	1
D. Duration of symptoms§§	
<6 weeks	0
≥6 weeks	1

Figure 13: ACR criteria[75]

ACR response criteria

1. ≥20% improvement in swollen joint count
2. ≥20% improvement in tender joint count
3. ≥20% improvement in at least 3 of the following 5 measures:
   A. Patient's global assessment of disease activity
   B. Physician's global assessment of disease activity
   C. Patient's assessment of pain
   D. Acute-phase reactant
   E. Disability

Figure 14: ACR response criteria [109]

Table 4. Proposed criteria* for complete clinical remission in rheumatoid arthritis†

Five or more of the following requirements‡ must be fulfilled for at least 2 consecutive months:§

1. Duration of morning stiffness not exceeding 15 minutes
2. No fatigue
3. No joint pain (by history)
4. No joint tenderness or pain on motion
5. No soft tissue swelling in joints or tendon sheaths
6. Erythrocyte sedimentation rate (Westergren method) less than 30 mm/hour for a female or 20 mm/hour for a male

* These criteria are intended to describe either spontaneous remission or a state of drug-induced disease suppression, which simulates spontaneous remission.

† To be considered for this designation a patient must have met the ARA criteria for definite or classic rheumatoid arthritis at some time in the past.

‡ No alternative explanations may be invoked to account for the failure to meet a particular requirement. For instance, in the presence of knee pain, which might be related to degenerative arthritis, a point for "no joint pain" may not be awarded.

§ Exclusions: Clinical manifestations of active vasculitis, pericarditis, pleuritis or myositis, and unexplained recent weight loss or fever attributable to rheumatoid arthritis will prohibit a designation of complete clinical remission.

Figure 15: ACR remission criteria [110]

HEALTH ASSESSMENT QUESTIONNAIRE

The Health Assessment questionnaire is based on the self-assessment of the patient. Limitations in daily life can be identified.

Questions about different areas of operations are asked:

- Dressing and grooming
- Arising
- Eating
- Walking
- Hygiene
- Reach
- Grip
- Activities

All areas include questions about devices used or help from other persons needed.

The HAQ also included questions about the medical history, medical conditions, health status and health activities, exercise and medications [111].

RHEUMATOID ARTHRITIS DISEASE ACTIVITY INDEX (RADAI)

The RADAI is a self-administered questionnaire to access disease activity.

RADAI item
Numerical rating scale questions (0–10 scale)
1. In general, how active has your arthritis been over the past 6 months?
2. In terms of joint tenderness and swelling, how active is your arthritis today?
3. How much arthritis pain do you feel today?
Likert scale question (0–6 scale)
4. Were your joints stiff when you woke up today? If yes, how long did this extra stiffness last?
no = 0; <30 minutes = 1; 30 minutes to an hour = 2; 1–2 hours = 3; 2–4 hours = 4; >4 hours = 5; all day = 6
Joint list question (sum score range 0–48; 8 joints or joint groups on both sides of the body, each graded 0–3)
5. Please indicate the amount of pain you are having today in each of the joint areas listed below
None = 0; mild = 1; moderate = 2; severe = 3
Shoulders, elbows, wrists, fingers, hips, knees, ankles, and toes

Figure 16: RADAI index [112]

DISEASE ACTIVITY SCORE (DAS)

The DAS is used to measure disease activity. A commonly used score is the DAS 28, which assesses 28 joints that are affected by rheumatoid arthritis. The number of swollen joints, erythrocyte sedimentation rate (ESR) and/or C reactive protein (CRP) and the patient's global assessment of health are included and give the overall disease activity score. The score is divided into three categories [113]:

- > 5.1. implies high disease activity
- 3.2 – 5.1 implies moderate disease activity
- 2.6 – 3.2 implies low disease activity
- < 2.6 implies remission [114]

RADIOLOGIC PROGRESSION (SHARP AND LARSEN METHOD

The Sharp and Larsen method are used to access radiologic progression in rheumatoid arthritis.

According to Larsen, 5 grades of radiologic changes can be identified:

- 0 no pathologic indication
- 1 unspecified pathologic changes
- 2 minor, but certain destructive changes
- 3 moderate destructive changes
- 4 major destructive changes
- Multiple destructive changes

The joints of the hand are rated separately on erosion, joint space narrowing, soft-tissue swelling and osteoporosis near the joint[115].

The Sharp method modified by van der Heijde includes 16 areas of both hands and wrist, as well as the MTP's and two intraphalangeal joints to develop an erosion score.

- 0 Normal
- 1 discrete erosions
- 2-3 larger erosions according to surface area involved
- 4 erosions extending over middle of the bone
- 5 complete collapse

The maximum erosion score for the hands is 160 and 120 for the feet. Maximum joint space narrowing score is 120 for the hands and 48 for the feet. The total score ranges from 0 to 448[116].

WHO-ILAR CORE SET

The WHO/ ILAR Core domains for longitudinal observational studies define a core set of domains and reporting requirements for these studies:

- Health Status
- Disease progress
- Damage
- Mortality
- Toxicity/Adverse Reactions [117]

SIMPYLFIED DISEASE ACTIVITY INDEX (SDAI)

The SDAI combines swollen joint counts, tender joint counts, patient global assessment, physician global assessment and CRP (mg/dl) in a numeric summation[118]. The overall SDAI score should be interpreted as follow:

- 0.0 – 3.3. Remission
- 3.4 – 11.0 Low Activity
- 11.1 – 26.0 Moderate Activity
- 26.1 – 86.0 High Activity [119]

CLINICAL DISEASE ACTIVITY INDEX (CDAS)

The CDAS is calculated on basis of a tender joint score, swollen joint score, patient global score and provider global score.

The score can be interpreted as follows:

- 0.0 – 2.8 Remission
- 2.9 – 10.0 Low Activity
- 10.1 – 22.0 Moderate Activity
- 22.1 – 76.0 High Activity [120]

Score sheet for the OMERACT RAMRIS

using the EULAR-OMERACT RA MRI reference image atlas

MCP JOINTS

MRI ID: _____ **Scorer's name:** _____

Centre where MRI was performed: _____

Image set (e.g. baseline or follow-up): _____

Sequences scored: _____

Scoring of synovitis

	MCP-joints			
	2	3	4	5
Synovitis (0-3)				

Scoring of bone erosion and bone oedema

Bone erosion is scored 0-10, according to the proportion (in increments of 10%) of bone involved:
0: 0%, 1: 1-10%, 2: 11-20 %, ……., 10: 91-100%

Bone oedema is scored 0-3, according to the proportion (in increments of 33%) of bone involved:
0: 0%, 1: 1-33%, 2: 34-66 %, 3: 67-100%

Score from the articular surface (or its best estimated position if absent) to a depth of 1 cm.

		MCP joints			
		2	3	4	5
Bone erosion 0-10	Proximal				
	Distal				
Bone oedema 0-3	Proximal				
	Distal				

Score sheet for the OMERACT RAMRIS

using the EULAR-OMERACT RA MRI reference image atlas

WRIST JOINTS

MRI ID: _____ **Scorer's name:** _____

Centre where MRI was performed: _____

Image set (e.g. baseline or follow-up): _____

Sequences scored: _____

Scoring of synovitis

	Distal radio-ulnar joint	Radio-carpal joint	Intercarpal-CMCJ
Synovitis (0-3)			

Scoring of bone erosion and bone oedema

Bone erosion is scored 0-10, according to the proportion (in increments of 10%) of bone involved:
0: 0%, 1: 1-10%, 2: 11-20 %, ……., 10: 91-100%

Bone oedema is scored 0-3, according to the proportion (in increments of 33%) of bone involved:
0: 0%, 1: 1-33%, 2: 34-66 %, 3: 67-100%

For carpal bones, score the whole bone. For long bones, score from the articular surface (or its best estimated position if absent) to a depth of 1 cm.

	Base of metacarpal				
	1	2	3	4	5
Bone erosion (0-10)					
Bone oedema (0-3)					

	Trapezium	Trapezoid	Capitate	Hamate
Bone erosion (0-10)				
Bone oedema (0-3)				

	Scaphoid	Lunate	Triquetrum	Pisiform
Bone erosion (0-10)				
Bone oedema (0-3)				

	Distal radius	Distal ulna
Bone erosion (0-10)		
Bone oedema (0-3)		

Figure 17: Example of score sheets for scoring MCP joints and wrist joints with the OMERACT RAMRIS criteria [121]

EULAR RECOMMENDATIONS FOR MANAGEMENT OF EARLY ARTHRITIS

1. Arthritis is characterised by the presence of joint swelling, associated with pain or stiffness. Patients presenting with arthritis of more than one joint should be referred to, and seen by, a rheumatologist, ideally within six weeks after the onset of symptoms.
2. Clinical examination is the method of choice for detecting synovitis. In doubtful cases, ultrasound, power Doppler, and MRI might be helpful to detect synovitis.
3. Exclusion of diseases other than rheumatoid arthritis requires careful history taking and clinical examination, and ought to include at least the following laboratory tests: complete blood cell count, urinary analysis, transaminases, antinuclear antibodies.
4. In every patient presenting with early arthritis to the rheumatologist, the following factors predicting persistent and erosive disease should be measured: number of swollen and tender joints, ESR or CRP, levels of rheumatoid factor and anti-CCP antibodies, and radiographic erosions.
5. Patients at risk of developing persistent or erosive arthritis should be started with DMARDs as early as possible, even if they do not yet fulfil established classification criteria for inflammatory rheumatological diseases.
6. Patient information concerning the disease and its treatment and outcome is important. Education programmes aimed at coping with pain, disability, and maintenance of work ability may be employed as adjunct interventions.
7. NSAIDs have to be considered in symptomatic patients after evaluation of gastrointestinal, renal, and cardiovascular status.
8. Systemic glucocorticoids reduce pain and swelling and should be considered as adjunctive treatment (mainly temporary), as part of the DMARD strategy. Intra-articular glucocorticoid injections should be considered for the relief of local symptoms of inflammation.
9. Among the DMARDS, methotrexate is considered to be the anchor drug, and should be used first in patients at risk of developing persistent disease.
10. The main goal of DMARD treatment is to achieve remission. Regular monitoring of disease activity and adverse events should guide decisions on choice and changes in treatment strategies (DMARDs including biological agents).
11. Non-pharmaceutical interventions such as dynamic exercises, occupational therapy, and hydrotherapy can be applied as adjuncts to pharmaceutical interventions in patients with early arthritis.
12. Monitoring of disease activity should include tender and swollen joint count, patient's and physician's global assessments, ESR, and CRP. Arthritis activity should be assessed at one to three month intervals, for as long as remission is not achieved. Structural damage should be assessed by radiographs of hands and feet every 6 to 12 months during the first few years. Functional assessment (for example, HAQ) can be used to complement the disease activity and structural damage monitoring.

Figure 18: EULAR recommendations for management of early arthritis [122]

EULAR RECOMMENDATIONS FOR THE USE OF IMAGING OF THE JOINTS IN THE CLINICAL MANAGEMENT OF RHEUMATOID ARTHRITIS

Table 1 Recommendations, SOR and level of evidence

	Recommendation*	SOR, mean VAS0–10 (95% CI)	Level of evidence
1	When there is diagnostic doubt, CR, ultrasound or MRI can be used to improve the certainty of a diagnosis of RA above clinical criteria alone†	9.1 (8.6 to 9.6)	III
2	The presence of inflammation seen with ultrasound or MRI can be used to predict the progression to clinical RA from undifferentiated inflammatory arthritis	7.9 (6.7 to 9.0)	III
3	Ultrasound and MRI are superior to clinical examination in the detection of joint inflammation; these techniques should be considered for more accurate assessment of inflammation	8.7 (7.8 to 9.7)	III
4	CR of the hands and feet should be used as the initial imaging technique to detect damage. However, ultrasound and/or MRI should be considered if conventional radiographs do not show damage and may be used to detect damage at an earlier time point (especially in early RA)	9.0 (8.4 to 9.6)	IV
5	MRI bone oedema is a strong independent predictor of subsequent radiographic progression in early RA and should be considered for use as a prognostic indicator. Joint inflammation (synovitis) detected by MRI or ultrasound as well as joint damage detected by conventional radiographs, MRI or ultrasound can also be considered for the prediction of further joint damage	8.4 (7.7 to 9.2)	III
6	Inflammation seen on imaging may be more predictive of a therapeutic response than clinical features of disease activity; imaging may be used to predict response to treatment	7.8 (6.7 to 8.8)	III-IV
7	Given the improved detection of inflammation by MRI and ultrasound than by clinical examination, they may be useful in monitoring disease activity	8.3 (7.4 to 9.1)	III
8	The periodic evaluation of joint damage, usually by radiographs of the hands and feet, should be considered. MRI (and possibly ultrasound) is more responsive to change in joint damage and can be used to monitor disease progression	7.8 (6.8 to 8.9)	III
9	Monitoring of functional instability of the cervical spine by lateral radiograph obtained in flexion and neutral should be performed in patients with clinical suspicion of cervical involvement. When the radiograph is positive or specific neurological symptoms and signs are present, MRI should be performed	9.4 (8.9 to 9.8)	III
10	MRI and ultrasound can detect inflammation that predicts subsequent joint damage, even when clinical remission is present and can be used to assess persistent inflammation	8.8 (8.0 to 9.6)	III

*Recommendations are based on data from imaging studies that have mainly focused on the hands (particularly wrists, metacarpophalangeal and proximal interphalageal joints). There are few data with specific guidance on which joints to image.
†In patients with at least one joint with definite clinical synovitis, which is not better explained by another disease.
Categories of evidence: Ia, evidence for meta-analysis of randomised controlled trials; Ib, evidence from at least one randomised controlled trial; IIa, evidence from at least one controlled study without randomisation; IIb, evidence from at least one other type of quasi-experimental study; III, evidence from non-experimental descriptive studies, such as comparative studies, correlation studies and case–control studies; IV, evidence from expert committee reports or opinions or clinical experience of respected authorities, or both.
CR, conventional radiography; RA, rheumatoid arthritis; SOR, strength of recommendation; VAS, visual analogue scale (0–10; 0=not recommended at all, 10=fully recommended).

Figure 19: EULAR recommendations for the use of imaging of the joints in the clinical management of rheumatoid arthritis [58]

SWOT MAGNETE RESONANCE IMAGING (MRI)

STRENGTHS	WEAKNESSES
Safe - No ionizing radiation - Non-invasive **Patient comfort** - painless **RA signs** - Synovitis - Bone Marrow Oedema - Cartilage, ligaments, tendons and tendon sheaths - Intra- and extra- articular fluid collections **Monitoring** - Treatment response **Position** - Established **Global view** - Articular surfaces - Internal bone structure **Procedure** - Outpatient **Scoring** - Scoring criteria available	**Availability** **Costs** - High costs **Interpretation** - Complex - Inter observer variability - Operator dependent **Time** - 15-90 minutes per scan - Time between scan and results - Waiting lists **Unsafe** - Contrast dye **Patient comfort** - Time - Claustrophobia **Image quality** - Motion Artefacts - Low resolution in comparison with ultrasound **Contraindications** - Implants **Measurements multiple parts** - Wrist, MCP,PIP and DIP joints cannot be examined with equal high resolution at the same time - Too time consuming and expensive
OPPORTUNITIES	THREATS
Application areas - 1st and 2nd line - Clinical trials **Data storage** - Stored and read centrally **Prognostication** **New forms** - Gadolinium – enhanced MRI - Diffusion – weighted MRI - 3D MRI datasets linked to ultrasound examination in real-time - Dedicated extremity MRI units **Guidelines**	**Other (new) devices**

Figure 20: SWOT MRI [60, 123-131]

STRENGHTS	WEAKNESSES
Availability **Costs** - Low costs **Patient comfort** - Painless - Interactive **Safe** - Non-invasive - No ionizing radiation **Monitoring** - Treatment response **Global view** - Assessment of multiple joint sites **Procedure** - Outpatient **Data storage** - Recordable **Real time** **Time** - Duration scan 15-45 minutes **Reproducibility** **Ra signs** - Assessment of synovitis (thickening synovial membrane, bursae or tendon sheaths, increased synovial blood flow) - Fluid in joints, bursae and tendon sheaths **Position** - Mainly established	**Interpretation** - Complex - Inter observer variability - Operator dependent - Long learning curve for inexperienced operator - Poor objective documentation - Reproducibility problems **RA signs** - Changes in the bone difficult to access - Internal bone structure not visualized - Bone marrow oedema cannot be assessed **Position** - Limited testing on systems in longitudinal follow-up studies **Image quality** - Site dependant **Monitoring** - Relative advantage of Ultrasound over X-ray for showing erosive progression is unclear
OPPORTUNITIES	THREATS
New forms - Use of Portable ultrasound machines (No appointment with radiologist needed) - Miniaturization of devices **Guidelines** - EULAR guidelines for the use of musculoskeletal Ultrasound in rheumatology **Application areas** - Imaging studies - 1st and 2nd line - Guide invasive joint procedures **Prognostication** **Scoring**	**Other (new) devices**

Figure 21: SWOT Ultrasound [123, 128-130]

STRENGHTS	WEAKNESSES
Availability **Costs** - Low costs **Patient comfort** - Painless **Safe** - Non-invasive **Procedure** - Outpatient **Position** - "Gold standard" - Validated assessment methods **Monitoring** - Later stages (changes in joint space and bone erosion) **RA signs** - Joint subluxations, malalignment and/or ankylosis in severe cases - Juxta-articular osteoporosis and cysts - Bone erosion - Joint space narrowing **Data storage** - Standardized and blinded centralized reading possible **Reproducibility** **Differentiation** - From other joint conditions e.g. osteoarthritis, psoriatic arthritis, neoplasm **Scoring**	**Availability** - Performed by radiographer in radiology department **Unsafe** - Radiation **Monitoring** - Intermediate term follow up of treatment **RA signs** - No visualization of synovium and cartilage(soft tissue changes) in early stages - Low sensitivity to early bone erosion - No visualization of ligaments **Interpretation** - Inter observer variability **Image quality** - Projectional superimposition **Non-progressors**
OPPORTUNITIES	THREATS
	Other (new) devices **Miniaturization of devices** **Guidelines**

Figure 22: SWOT X-ray [65, 123, 125, 132]

SWOT CT-SCAN

STRENGHTS	WEAKNESSES
Image quality - Clearer than standard x-ray **Procedure** - Outpatient **RA signs** - Displays blood vessels - More sensitive to calcified tissue (bone erosions) than MRI **Time** - Examination 1 minute for hand and wrist	**Unsafe** - Radiation - Contrast dye (sometimes) **Image quality** - Motion artefacts **Availability** - Only in centres - Rarely used in clinical practice **Time** - Time between scan and results **Contraindications** - Pregnancy, metal items **RA signs** - Low sensitivity to soft tissue changes in comparison with MRI and Ultrasound **Rarely used in clinical practice**
OPPORTUNITIES	THREATS
New forms - MDCT scan (Three-dimensional visualization of joints)	**Other (new) devices** **Miniaturization of devices**

Figure 23: SWOT CT-scan [123]

APPENDIX E

DEFINITION MEDICAL DEVICE

Medical device: “A Medical device means any instrument, apparatus, implement, machine appliance, implant, in vitro reagent or calibrator, software, material or other similar or related article, intended by the manufacturer to be used, alone or in combination, for human beings for one or more of the specific purposed of:

- diagnosis, prevention, monitoring, treatment or alleviation of disease
- diagnosis, monitoring, treatment, alleviation of or compensation for an injury
- investigation, replacement, modification, or support of the anatomy or of a physiological process
- supporting or sustaining life
- control of conception
- disinfection of medical devices
- providing information for medical purposes by means of in vitro examination of specimens derived from the human body and which does not achieve its primary intended action in or on the human body by pharmacological, immunological or metabolic means, but which may be assisted in its function by such means.” [133]

MODE, RANGE, MINIMUM AND MAXIMUM OF THE IMPORTANCE OF THE CHARACTERISTICS

	Mode	Range	Min	Max
Sensitivity	5	3	2	5
Specificity	5	4	1	5
Quality of the images	4	2	3	5
Duration scan	4	3	2	5
Assessment of big joints	4	3	2	5
Visualization of blood vessels	4	4	1	5
Visualization of (damaged) bone and cartilage	4	2	3	5
Visualization of tendons and ligaments	4	3	2	5
Subjective quantification of effect of therapy	4	3	2	5
Objective quantification of effect of therapy	4	4	1	5

Figure 25: Mode, range, minimum and maximum of the importance of the characteristics for imaging devices based on the questionnaire

	Mode	Range	Min	Max
Sensitivity	4	2	3	5
Specificity	4	2	3	5
Quality of the images	4	2	3	5
Duration scan	4	3	1	4
Assessment of big joints	4	2	3	5
Visualization of blood vessels	4[1]	2	2	4
Visualization of (damaged) bone and cartilage	4	2	3	5
Visualization of tendons and ligaments	4	2	3	5
Subjective quantification of effect of therapy	3	2	2	4
Objective quantification of effect of therapy	3	3	2	5

1) More than one mode. 2nd mode is 3

Figure 26: Mode, range, minimum and maximum of the importance of satisfaction MRI based on the questionnaire

	Mode	Range	Min	Max
Sensitivity	4	2	3	5
Specificity	4	2	3	5
Quality of the images	4	3	2	5
Duration scan	4	3	2	5
Assessment of big joints	4	2	3	5
Visualization of blood vessels	4	3	2	5
Visualization of (damaged) bone and cartilage	4	3	2	5
Visualization of tendons and ligaments	4	2	3	5
Subjective quantification of effect of therapy	3	3	2	5
Objective quantification of effect of therapy	3	3	1	4

Figure 27: Mode, range, minimum and maximum of the importance of satisfaction Ultrasound based on the questionnaire

	Mode	Range	Min	Max
Sensitivity	4	3	2	5
Specificity	4	2	2	4
Quality of the images	4	3	2	5
Duration scan	4	2	3	5
Assessment of big joints	4	3	2	5
Visualization of blood vessels	1	3	1	4
Visualization of (damaged) bone and cartilage	3	3	2	5
Visualization of tendons and ligaments	1	3	1	4
Subjective quantification of effect of therapy	3	4	1	5
Objective quantification of effect of therapy	3	3	1	4

Figure 28: Mode, range, minimum and maximum of the importance of satisfaction X-ray based on the questionnaire

	Mode	Range	Minimum	Maximum
Sensitivity	4	2	3	5
Specificity	4	1	3	4
Quality of the images	4	2	3	5
Duration scan	4	2	2	4
Assessment of big joints	4	1	3	4
Visualization of blood vessels	3	3	1	4
Visualization of (damaged) bone and cartilage	3	1	3	4
Visualization of tendons and ligaments	3	3	1	4
Subjective quantification of effect of therapy	3	2	2	4
Objective quantification of effect of therapy	3	2	2	4

Figure 29: Mode, range, minimum and maximum of the importance of satisfaction CT-scan based on the questionnaire