Background to and outline of the OARSI treatment guidelines

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Overview of the OARSI treatment guidelines

Kawaguchi: This roundtable discussion is on the Osteoarthritis Research Society International (OARSI) treatment guidelines, of which part 1 has just been published this year and part 2 on consensus recommendations will be published early in 2008.

First of all, please could you give a brief outline of the OARSI treatment guidelines, especially in comparison with the former osteoarthritis (OA) guidelines issued by the European League Against Rheumatism (EULAR) and American College of Rheumatology (ACR)?

Nuki: In its format and approach the OARSI guidelines for the treatment of hip and knee OA in many ways modeled on the recent EULAR guidelines. It was felt that there was not only a need for updated guidelines but also for core guidelines that were more globally relevant. The OARSI guidelines were developed for physicians in both primary and secondary care and for allied health professionals who work with such physicians, and surgeons. In addition, it was hoped that they would be of value for patients as well.

The project was begun at OARSI's request in 2005 with a view to publishing the guidelines at the end of 2007. So as not to duplicate previous work, the systematic reviews of the scientific literature up to 2002 which had formed the evidence base for the EULAR guidelines were accepted, and a systematic review of the more recent evidence which had emerged up until January 2006 was performed. Simultaneously, a critical appraisal of the existing guidelines, which had not been done before, was undertaken. It was found that there were 23 evidence-based guidelines or national society consensus documents from around the world that were relevant to the treatment of OA of the hip/knee. The various treatment modalities considered in these guidelines were categorized according to the extent of agreement on their usefulness and by the level of evidence available to support each of them as shown in **Table 1**.

The EULAR and OARSI recommendations were, however, developed in rather different ways. In the former case a group of European experts initially proposed what they considered were the key treatment recommendations, and this was followed by a systematic review of the evidence which might support or refute these recommendations. The OARSI guidelines, on the other hand, were developed the other way round. Whereas the EULAR guidelines were clinically led and evidence-supported, OARSI's were evidence-led and clinically supported. That is to say that the OARSI committee first examined the results of the systematic review of the evidence from trials in 2002-06, and the critical appraisal of existing guidelines, and then proceeded to produce a set of treatment propositions on which consensus was reached by a Delphi exercise. After 4 initial rounds of the Delphi process a set of provisional draft guidelines was presented to the OARSI membership for comments and suggestions. Following this feedback the guideline development group finally reached consensus on 25 carefully worded treatment propositions relating to a variety of pharmacological, non-pharmacological, and surgical therapeutic modalities, after two further rounds of the Delphi process. The strength of recommendation for each of the propositions was determined by votes of the committee of experts using a simple visual analog scale.

The other important differences between the EULAR and OARSI guidelines related to the extent of stakeholder involvement in their production. The European guidelines were intended essentially for European rheumatologists and surgeons whereas OARSI's were intended to be relevant for a wider constituency. Although not as international as they might have been, experts from six countries in two continents were involved in the development of the OARSI guidelines. The OARSI guideline development group was also a little more multidisciplinary in its composition than the taskforces that developed the EULAR recommendations, as it included two experts from primary care in addition to 14 specialists from rheumatology, orthopedics and evidence-based medicine. On the other hand the OARSI development committee included only one orthopedic surgeon, which I am sure would be a surprise for people in Japan, where so much of rheumatology is undertaken by orthopedic surgeons.

Differences in the treatment of OA in Japan and the USA or Europe

Kawaguchi: Although Japan was not one of the aforementioned six participating countries, these guidelines do cover the non-pharmacological and pharmacological treatments that are given in Japan today. On the other hand, however, the situation regarding the treatment of OA in Japan and the USA or Europe is quite different in terms of medical insurance,

1 OARSI recommendations for the management of hip and knee osteoarthritis, Part I: critical appraisal of existing treatment guidelines and systematic review of current research evidence. *Osteoarthritis and Cartilage* 2007, 15: 981-1000.

2 OARSI recommendations for the management of hip and knee osteoarthritis, Part II: OARSI evidence-based, expert consensus guidelines. *Osteoarthritis and Cartilage* 2008, 16: 137-162.

because in Japan the entire population is covered by social insurance, but only as regards treatment given at hospitals by doctors. Therefore when people experience joint pain due to OA, half go to hospital and consult a doctor and half seek alternative treatments elsewhere, because due to the numbers of patients covered hospital waiting times can be quite long in Japan. And since practices outside the hospitals are not socially insured and not allowed to use pharmacological treatments, alternatively they prescribe acupuncture, braces, insoles, or transcutaneous electrical nerve stimulation (TENS) with water-based exercise. This includes treatment with glucosamine and chondroitin sulfate, which are generally not regarded as drugs but as nutritional supplements in Japan.

In the hospital setting, doctors often recommend strengthening exercise and patient education. If the pain does not go away, NSAIDs are usually prescribed. However, most NSAIDs available in Japan are non-selective. Celecoxib was only approved in 2007. To most Japanese doctors, NSAIDs are simply NSAIDs regardless of their COX-2 selectivity. When NSAIDs do not work well, intra-articular (IA) injections are usually performed; steroid in cases in which there are signs of inflammation, otherwise hyaluronate. If this does not solve the problem, surgery is considered. That is the full story of treatment in Japan.

From an international point of view, what are the differences between Japanese strategies and those of other countries?

Nuki: The most notable differences result from the fact that half the patients in Japan are seen immediately by a hospital specialist. Because of the large numbers of patients with OA, the vast majority of patients in Europe and the USA are seen exclusively by physicians in primary care.

Another difference that I have noted is that in Japan IA injections of hyaluronan are much more widely prescribed for OA of the knee, and at a much earlier stage than they are in Europe and the USA. Also, whereas in Europe and North America there is almost unanimous agreement that the analgesic of first choice should be acetaminophen ≤4 g/day, this I believe is not the case in Japan because of concerns about hepatic toxicity.

Kawaguchi: Yes–we used to use it but these days we start with NSAIDs.

Nuki: In Europe the reverse is true largely because of concerns about gastrointestinal (GI) side effects of NSAIDs, and more recent concern about their potential for cardiovascular (CV) side

Table 1. Agreement and level of evidence for modalities of therapy recommended by existing guidelines*

Quoted from *Osteoarthritis and Cartilage* 2007, 15: 981-1000. Table IV [1]

Level of evidence†	Agreement (number of guidelines recommending the modality/total number of guidelines addressing the modality)				
	<25%	≥25%	≥50%	≥75%	100%
Ia	Ultrasound (1/5)	Chondroitin sulfate (2/7)	Heat/ice (7/10) Glucosamine sulfate (6/10) NSAID + H_2-blockers (5/8)	NSAIDs (15/16) Insole (12/13)‡ Braces (8/9)‡ Topical capsaicin (8/9)‡ IA hyaluronate (8/9)‡ IA steroid (11/13)‡ TENS (8/10) Topical NSAIDs (7/9)‡	Aerobic exercise (21/21) Strengthening exercise (21/21) Acetaminophen (16/16) Education (15/15) COX-2 inhibitors (11/11) Opioid (9/9) Self-management (8/8) Water-based exercise (8/8) NSAID + PPI (8/8) NSAID + misoprostol (8/8) Telephone (2/2)
Ib	Laser (1/6) Electrotherapy/EMG (1/8)	Nutrients (1/3)	Acupuncture (5/8) Massage (1/2) Diacerein (1/2)	Weight loss (13/14) Patellar tape (12/13) Avocado soybean unsaponifiables (3/4)	Combination therapy (12/12) Joint lavage (3/3) Herbs (2/2)
III					TJR (14/14) Osteotomy (10/10)
IV	Oral steroid (0/2)			Arthroscopic debridement (5/6)	Cane/stick (11/11)‡ Referral (5/5) Knee fusion (2/2)‡ Knee aspiration (2/2)‡

H_2-blocker: histamine type 2 receptor antagonist; TENS: transcutaneous electrical nerve stimulation; EMG: electromyography; PPI: proton pump inhibitor; TJR: total joint replacement.

* Modalities were grouped according to strength of agreement and level of evidence. Modalities addressed by only one guideline were not included, such as radiotherapy, sauna/spa, gait aid, topical rubefacients, estrogen, patellar resurfacing, and anti-depressants. Modalities not directly related to the treatment such as consideration of risk factors, clinical features, etc. were excluded.

† Level of evidence: Ia = systematic review of RCTs; Ib = RCT; IIa = controlled trial; IIb = quasi-experimental; III = cohort/case-control study; and IV = expert opinion. Only the highest level of evidence has been selected for each modality.

‡ Specific for knee OA.

effects (**Table 2**). As a result acetaminophen is mostly used initially, even though available evidence clearly suggests that in the majority of patients NSAIDs might be more effective.

Treatment consensus of the OARSI guidelines

Kawaguchi: OARSI recommendations for the management of hip and knee OA by pharmacological modalities of treatment are shown in **Table 3**.

According to it, the use of acetaminophen has a >90% strength of recommendation as an initial analgesic. NSAIDs should be used at the lowest effective dose, and their long-term use avoided if possible. In patients with increased GI risk, either a COX-2 selective agent or a non-selective NSAID plus a proton pump inhibitor or misoprostol for gastroprotection may be considered. NSAIDs should be used with caution in patients with a history of CV events.

What do you think about the CV risk associated with COX-2 inhibitors? Is this a class effect of NSAIDs or specific to coxibs?

Nuki: This remains an area of considerable controversy. The OARSI recommendations are that all selective COX-2 inhibitors, without distinction between so-called 'specific' and 'highly selective' ones, should be avoided in people with CV disease. There are, however, new data suggesting that the class

Table 2. Safety profiles: relative risk (RR) or odds ratio (OR) and 95%CI
Quoted from *Osteoarthritis and Cartilage* 2007, 15: 981-1000. Table VI [1]

Intervention*	Adverse events	RR/OR (95%CI)	Source of evidence
Acupuncture	Any	0.76 (0.13-4.42)	RCT
Acetaminophen	GI discomfort	0.80 (0.27-2.37)	RCTs
	GI perforation/bleed	3.60 (2.60-5.10)	CC
	GI bleeding	1.2 (0.8-1.7)	CCs
	Renal failure	0.83 (0.50-1.39)	CS
	Renal failure	2.5 (1.7-3.6)	CC
NSAIDs	GI perforation/ulcer/bleed	5.36 (1.79-16.10)	RCTs
	GI perforation/ulcer/bleed	2.70 (2.10-3.50)	CSs
	GI perforation/ulcer/bleed	3.00 (2.70-3.70)	CCs
	Myocardial infarction	1.09 (1.02-1.15)	CSs
Topical NSAIDs	GI events	0.81 (0.43-1.56)	RCTs
	GI bleed/perforation	1.45 (0.84-2.50)	CC
H_2-blocker + NSAID vs NSAID	Serious GI complications	0.33 (0.01-8.14)	RCTs
	Symptomatic ulcers	1.46 (0.06-35.53)	RCTs
	Serious CV or renal events	0.53 (0.08-3.46)	RCTs
PPI + NSAID vs NSAID	Serious GI complications	0.46 (0.07-2.92)	RCTs
	Symptomatic ulcers	0.09 (0.02-0.47)	RCTs
	Serious CV or renal events	0.78 (0.10-6.26)	RCTs
Misoprostol + NSAID vs NSAID	Serious GI complications	0.57 (0.36-0.91)	RCTs
	Symptomatic ulcers	0.36 (0.20-0.67)	RCTs
	Serious CV or renal events	1.78 (0.26-12.07)	RCTs
	Diarrhea	1.81 (1.52-2.61)	RCTs
COX-2 inhibitors			
Coxibs vs NSAID	Serious GI complications	0.55 (0.38-0.80)	RCTs
	Symptomatic ulcers	0.49 (0.38-0.62)	RCTs
	Serious CV or renal events	1.19 (0.80-1.75)	RCTs
Celecoxib	Myocardial infarction	2.26 (1.0-5.1)	RCTs
	Myocardial infarction	0.97 (0.86-1.08)	CSs/CCs
Rofecoxib	Myocardial infarction	2.24 (1.24-4.02)	RCTs
	Myocardial infarction	1.27 (1.12-1.44)	CSs/CCs
Valdecoxib	CV events	2.3 (1.1-4.7)	RCTs
Opioids	Any	1.4 (1.3-1.6)	RCTs
	Constipation	3.6 (2.7-4.7)	RCTs
Glucosamine sulfate	Any	0.97 (0.88-1.08)	RCTs
Diacerein	Diarrhea	3.98 (2.90-5.47)	RCTs

H_2-blocker: histamine type 2 receptor antagonist; PPI: proton pump inhibitor.
CC: case-control study; CS: cohort study. Pooled RR/OR was provided if more than one study were included.
* Compared with placebo/non-exposure unless otherwise stated.

effect may be much wider and might include all NSAIDs.Therefore all these agents should be used with caution and, if possible, avoided in people who have CV risk.

Kawaguchi: Do you know the American Heart Association (AHA) statement advocating very strict restrictions on the use of not only COX-2 inhibitors but also the entire class of NSAIDs?

Nuki: Although the OARSI treatment guidelines committee were aware of the AHA's recommendations, they were also very conscious that many OA patients with some risk factors for CV disease do require treatment with analgesics for symptoms of pain associated with their disease.

Kawaguchi: Actually, the OARSI guidelines recommend that NSAIDs including both non-selective and COX-2-selective agents should be used only with caution in patients with CV risk factors (**Table 3**), which suggests that the authors consider that the risk of CV events is a class effect.

Nuki: Yes I agree. It is whether or not there is a higher CV risk associated with the use of all selective COX-2 inhibitors that is still controversial. Even though they should be used with great care, it does not necessarily mean that they should be avoided altogether.

Kawaguchi: Among non-pharmacological treatments, aerobic and strengthening exercise, education and self-management, water-based exercise, and telephone are recommended with 100% agreement (**Table 1**). Which of these modalities is most popular in the UK?

Nuki: We do not currently have good data on the frequency with which non-pharmacological modalities of therapy are recommended in the treatment of hip and knee OA in the UK. Although it is not necessarily the view of the OARSI committee as a whole, my own opinion is that non-pharmacological treatment modalities for OA are not given adequate emphasis in the UK. In most cases, patients with OA see their doctor in general practice for a very brief consultation, and are given a drug prescription. There is a need for greater emphasis on non-pharmacological therapies that have been shown in randomized controlled trials and meta-analyses to be effective. Even though the effect size is small they should be tried. Although there is currently no hard evidence to support the hypothesis that optimal management of OA of the hip and knee requires a combination

Table 3. OARSI recommendations for the management of hip and knee OA: pharmacological modalities of treatment
Quoted from *Osteoarthritis and Cartilage* 2008, 16: 137-162. Table I [2]

Proposition	Level of evidence	Strength of recommendation, % (95%CI)
Acetaminophen (up to 4 g/day) can be an effective initial oral analgesic for treatment of mild-to-moderate pain in patients with knee or hip OA. In the absence of an adequate response, or in the presence of severe pain and/or inflammation, alternative pharmacological therapy should be considered based on relative efficacy and safety, as well as concomitant medications and co-morbidities.	Ia (knee) IV (hip)	92 (88-99)
In patients with symptomatic hip or knee OA, NSAIDs should be used at the lowest effective dose but their long-term use should be avoided if possible. In patients with increased GI risk, either a COX-2 selective agent or a non-selective NSAID with co-prescription of a proton pump inhibitor or misoprostol for gastroprotection may be considered, but NSAIDs, including both non-selective and COX-2 selective agents, should be used with caution in patients with CV risk factors.	Ia (knee) Ia (hip)	93 (88-99)
Topical NSAIDs and capsaicin can be effective as adjunctives and alternatives to oral analgesic/anti-inflammatory agents in knee OA.	Ia (NSAIDs) Ia (capsaicin)	85 (75-95)
IA injections with corticosteroids can be used in the treatment of hip or knee OA, and should be considered particularly when patients have moderate-to-severe pain not responding satisfactorily to oral analgesic/anti-inflammatory agents and in patients with symptomatic knee OA with effusions or other physical signs of local inflammation.	Ib (hip) Ia (knee)	78 (61-95)
Injections of IA hyaluronate may be useful in patients with knee or hip OA. They are characterized by delayed onset, but prolonged duration, of symptomatic benefit when compared with IA injections of corticosteroids.	Ia (knee) Ia (hip)	64 (43-85)
Treatment with glucosamine and/or chondroitin sulfate may provide symptomatic benefit in patients with knee OA. If no response is apparent within 6 months treatment should be discontinued.	Ia (glucosamine) Ia (chondroitin)	63 (44-82)
In patients with symptomatic knee OA glucosamine sulfate and chondroitin sulfate may have structure-modifying effects while diacerein may have structure-modifying effects in patients with symptomatic OA of the hip.	Ib (knee) Ib (hip)	41 (20-62)
The use of weak opioids and narcotic analgesics can be considered for the treatment of refractory pain in patients with hip or knee OA, where other pharmacological agents have been ineffective or are contraindicated. Stronger opioids should only be used for the management of severe pain in exceptional circumstances. Non-pharmacological therapies should be continued in such patients and surgical treatments should be considered.	Ia (weak opioids) IV (strong opioids) IV (others)	82 (74-90)

of both pharmacological and non-pharmacological therapy, this is recommended in all existing guidelines, and was strongly recommended in the OARSI guidelines.

Kawaguchi: The 100% consensus suggests that in physicians' experience this combined approach seems attractive.

Nuki: Yes I agree but there are other instances where the strength of recommendation for a particular modality of treatment does not strictly follow the level of evidence for its efficacy. Take, for example, treatment with IA hyaluronan, which is characterized by delayed onset of action but prolonged duration of symptomatic benefit compared with IA injections of corticosteroids. If you look at **Table 1**, you will see that although the level of evidence for this is 1a–that is, there is evidence for efficacy from meta-analyses of randomized controlled trials for both OA of the knee and the hip–the strength of recommendation is nevertheless only 64% with a very wide confidence interval (**Table 3**). Why should that be if there is such good evidence? If you look more closely, you will see that although there have been several systematic reviews of IA hyaluronan therapy published over the last 3-4 years they have come to widely differing conclusions, because of heterogeneity of the compounds, different trial endpoints, and so on. It is clear that there was far from unanimous agreement about the value of IA hyaluronan when one looks into the evidence more deeply.

Kawaguchi: Orthopedic surgeons in Japan have very varying opinions regarding hyaluronan IA. Frankly, I feel that corticosteroid IA is more effective than hyaluronan IA, at least for acute symptoms. However, the level of recommendation for both these drugs is similar.

Nuki: When one looks at the strength of each recommendation it is important to look at the confidence limits of the recommendation, rather than simply at the mean value. It is also very important to realize that each recommendation relates to the carefully worded proposition itself, along with its caveats, and not to the modality of therapy as a whole. For example, in **Table 3** the statement that topical NSAIDs can be effective as adjuncts and alternatives to oral analgesic anti-inflammatory agents in knee OA is accompanied by a strength of recommendation relating to that general statement, rather than to any individual modality of therapy.

Kawaguchi: Many Japanese physicians and orthopedic surgeons are very interested in dietary supplements such as glucosamine and chondroitin sulfate. Even though almost all of these supplements are not regarded as medicines in Japan, they sell very well; many patients with knee and hip pain are taking them. What do you think about dietary supplements? In the OARSI guidelines, there is a high level of evidence, but agreement is lower than that for IA hyaluronan and, of course, coxibs (**Table 1**).

Nuki: There was initially a wide range of opinion among members of the committee. However, eventually all the recommendations achieved consensus, so I should explain how consensus was reached in the Delphi exercise. At each stage, if >60% of the committee accepted any proposition it was regarded as having reached consensus whereas if <20% agreed it was rejected out of hand. If 20-60% of the committee accepted any proposition, it was reconsidered and either reworded or amalgamated with another proposition until consensus was reached.

One must not confuse the level of consensus and strength of recommendation. For example, for glucosamine and chondroitin sulfate the available evidence from randomized controlled trials suggests some symptomatic benefits, although there was tremendous heterogeneity among the trials. One of the limitations of all guidelines is that they very quickly become out of date. Since the OARSI systematic review of the evidence finished in January 2006 the results of two important trials of glucosamine and chondroitin sulfate have been published. To see how the results from these later studies might influence the recommendations that had been made without them, the data from the later studies was entered into the calculations that had been made for effect size before the publication of those studies. As a result of this sensitivity analysis the conclusions with regard to the efficacy of glucosamine were not altered, but inclusion of the later data suggested that treatment with oral chondroitin sulfate might not have significant symptomatic benefit.

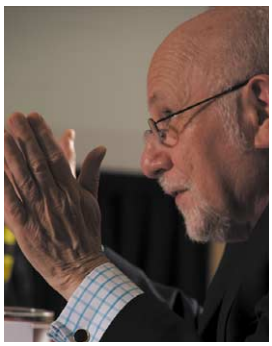
Kawaguchi: How often is it planned to update the guidelines in terms of publication?

Nuki: OARSI will review the evidence every year and then decide when the guideline recommendations need to be amended and published. It is anticipated that this might be after 2-5 years depending on what new evidence from clinical trials becomes available.

Dissemination of the guidelines

Kawaguchi: What is your plan for dissemination of the guidelines?

Nuki: Dissemination is extremely important and in addition to publication in *Osteoarthritis and Cartilage* OARSI is planning meetings to discuss the recommendations in collaboration with national societies representing stakeholders and potential users around the world. OARSI sees these recommendations as being core guidelines that can be adapted for use in accordance with regional and national needs and circumstances. For example it would not make sense to make a recommendation relating to a treatment modality that simply was not available in a certain country or locality; the OARSI guideline should also be adaptable for use in different care settings. We are aware that any guideline only stands a chance of being implemented if the people who are going to use it have some stake in its development and dissemination.



For this reason OARSI will reach out to various national organizations, specialist, societies, and so forth, including orthopedic surgeons, rheumatologists, other allied health professionals and even patient organizations. OARSI will encourage authentic translation into other languages. Initially OARSI will publish the guidelines in full, but it is also planned to produce an executive summary of the recommendations that can be sent to various stakeholder groups to help them to adapt the core recommendations to their own circumstances. OARSI is already start-

ing to consider having joint meetings with other national societies; one for European physicians is going to be held in Paris in February 2008, and there are plans to discuss the guidelines at the APLAR meeting in Yokohama in September 2008.

Possibility of disease-modifying treatment for OA

Kawaguchi: Do you think that we already have disease-modifying drugs instead of symptom-modifying drugs?

Nuki: The OARSI treatment guidelines committee accepted that there might be some structure-modifying effect using glucosamine sulfate, chondroitin sulfate, and diacerein–even though it did not recommend diacerein as a symptom-modifying drug. Whether or not any of the drugs currently used do truly have any disease-modifying effect remains very controversial. My own view, having reviewed the evidence, is that all the treatments that we currently have elicit at best only very modest structure-modifying effects. Although combination therapy might be a more effective approach, I think that everyone would agree that we badly need new agents that have much larger effect sizes. Of course, the modality of treatment that undoubtedly has the largest effect size for pain relief, increase in function and overall improvement in health-related quality of life, for patients with advanced disease, is joint replacement surgery. Joint replacements have also been demonstrated to be more cost-effective than the pharmacological agents available–in very selected groups of patients with severe and advanced disease.

Kawaguchi: In terms of future drugs, are there any that might possibly exert disease-modifying effects–for example, matrix metalloproteinase (MMP) inhibitors or some kind of signaling modulator?

Nuki: I don't think that current evidence allows any confident predictions. Nevertheless our increasing understanding of how genetic, biochemical and biomechanical factors can combine to lead to the development of OA is very exciting. In particular the rapidly developing knowledge of the role of cytokines, metalloproteinases, growth factors and signaling molecules in cartilage in experimental animal models of OA is pointing towards a number of rational potential new targets to be explored. However, since drug development is such a difficult and complex process I do not think that we can say right now whether a selective MMP or cytokine inhibitor, a growth factor or a signaling modulator has the best prospects for development as a safe and effective disease-modifying anti-osteoarthritic drug.

Kawaguchi: There are many signaling molecules involved in OA development and progression; extracellular molecules might possibly be better targets because it is very difficult to modulate intracellular molecules due to lack of carriers. Natural carriers such as a virus cannot be used clinically for the time being; hence it is very difficult to modulate intracellular signaling directly.

Nuki: I agree. One of the most exciting recent developments has been the ability to explore the role of specific genes and cartilage matrix molecules in mechanical models of OA pathogenesis in small laboratory animals. Perhaps the most promising recent example has been the work which has focused attention on the role of the aggrecanase ADAM-TS5. Experiments which demonstrated that knocking out the genes for these molecules could prevent the progression of mechanically induced experimental OA suggested that they could be potential targets for selective small-molecule inhibitors which might prove to be useful as disease-modifying pharmaceutical agents.

Kawaguchi: Even if disease-modifying drugs were to be developed, what do you think would be the best outcome measure to assess their efficacy in future?

Nuki: At the present time the regulatory agencies recommend that carefully controlled serial radiographs of joint space width are still the gold standard to determine changes in articular thickness. MRI has tremendous potential for detecting changes in cartilage structure and volume as well as other changes in joint structure in relatively shorter periods of time but the technology is not yet sufficiently refined or standardized to allow it to be substituted for well-conducted radiological studies.

There is also currently an OARSI/OMERACT initiative which aims to provide a set of criteria for considering total joint replacement as a clinical endpoint for evaluating potential disease-modifying drugs for OA.

Final remarks

Kawaguchi: Finally, do you have any message to Japanese physicians or orthopedic surgeons?

Nuki: Yes–a recommendation that I would like to pass on to Japanese physicians and surgeons is a recommendation that I would wish to pass on to physicians, surgeons and health professionals who deal with patients with hip and knee OA everywhere. In order to try to assess the possible influence of new consensus guidelines, there is a need to collect data on clinical outcomes before and after they are implemented. There is a need to audit current practice and outcomes in various care settings around the world. The first thing we need to know is how frequently the current OARSI recommendations are being implemented. In Europe and the USA many of the recommendations are not currently being offered to patients with OA in primary care settings and even in hospital orthopedic and rheumatology secondary care, patients with hip and knee OA are relatively overlooked and neglected by comparison with patients who have inflammatory arthritis.

Kawaguchi: Thank you very much for sharing your thoughts and insights with us today.