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Review

From joint anatomy to clinical outcomes in osteoarthritis and cartilage repair: summary of the fifth annual osteoarthritis imaging workshop

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SUMMARY

Objective: This white paper constitutes an overview of presentations and discussions from the fifth Annual Workshop on Imaging in Osteoarthritis (OA) held in Salzburg June eighth to eleventh 2011.
Design: This workshop brought together the communities of basic OA researchers, orthopedists and rheumatologists, imaging scientists, instrument manufacturers, and pharmaceutical representatives to focus on three overlapping themes of joint anatomy, cartilage repair and clinical validation of imaging biomarkers.
Results: The workshop was held on the campus of the Paracelsus Medical University in Salzburg, Austria from June 8–11, 2011; 133 attendees participated, representing 17 countries. The meeting was successful in facilitating discussion, raising awareness and consolidating knowledge about application of imaging in OA research studies and cartilage repair.
Conclusions: The OA research communities need to work alongside the regulatory, pharmaceutical, and MRI industries to support the new ideas and engage in the positive reinforcement of resources to further the new studies. A number of new initiatives were discussed to further break down obstacles to clinical trial utility of imaging biomarkers.

Osteoarthritis (OA) imaging workshops

The general goal of the Workshops on Imaging in OA, which has been endorsed by the Osteoarthritis Research Society International (OARSI) and taken place thus far in Ainring/Salzburg (Germany/Austria) in 2007, Boston (USA) in 2008, York (England) in 2009, and Vancouver (Canada) in 2011, is to promote technical developments and particularly applied research of *in vivo* imaging of OA, with a particular focus on the relations with clinical outcomes. Each workshop develops a (series of) theme(s) and delineates (1) what imaging science has contributed thus far, (2) what the pressing questions are and what imaging can help to address these and what resources and research agenda are needed to move forward. In addition to invited presentations and to podium discussions, the meetings include oral and poster sessions from submitted abstracts, one exclusively reserved for young investigators. Until this annual series of workshops began, there was no dedicated forum for interaction and collaborative development in this field necessary to bring together the critical mass for advancing this field.

These workshops come at a critical time in OA research, at which the mainstays of current OA management are analgesics and (total) joint replacement. Efforts to develop therapies to slow, halt or reverse the disease have been hampered by unresponsive measures of the disease process. Unprecedented investment (both industry and federally sponsored) is currently underway [i.e., the Osteoarthritis Initiative (OAI) and other large epidemiological studies] aimed at addressing this pressing concern and developing or qualifying new and responsive imaging markers. However, there is little consensus on which structural imaging changes are related to clinical outcomes (how a patient feels, functions or survives). Imaging biomarkers may improve the assessment of the onset, early development and progression of the disease, and could greatly facilitate evaluation of treatment efficacy in OA clinical trials. Foremost among these is magnetic resonance imaging (MRI), a non-invasive method for assessing joint morphology[1,2].

The fifth Annual Workshop

The goal of the fifth Annual Workshop was to bring together all stakeholders in the field, to focus on three overlapping themes: joint anatomy, cartilage repair and clinical validation of imaging biomarkers. The workshop was held on the campus of the Paracelsus Medical University (PMU) in Salzburg, Austria. From June

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8–11, 2011; 133 attendees participated (Fig. 1), representing 17 countries: four from Australia, 15 from Austria, two from Belgium, seven from Canada, four from Finland, one from France, 20 from Germany, five from Japan, two from Mexico, nine from the Netherlands, one from Norway, one from Spain, three from Sweden, 12 from Switzerland, seven from the UK, and 38 from the US. Of the 133 participants, 56 represented 25 companies active in the field.

The primary goals of the workshop were:

1. to promote discussion in the context of imaging biomarkers of OA,
2. to revisit human joint anatomy and to relate state-of-the-art imaging biomarkers to human joint anatomy,
3. to revisit imaging biomarkers of cartilage repair and present/discuss recent data on the relationship of cartilage repair, imaging biomarkers of cartilage repair, and clinical outcomes,
4. to present and discuss the most recent data on the relationship of imaging biomarkers and clinical outcomes in OA.

Pre-course in joint anatomy

This educational session was targeted at the full range of participants including those relatively naive to anatomy to experienced investigators who apply this knowledge daily. Fifty-six participants signed up and received small group, practical, hands-on tutorials on all major human joints (knee, hip, shoulder elbow, hand, foot) and the spine from anatomy tutors in the dissection labs of PMU. Participants were given the opportunity to study relevant structures such as the joint surfaces, ligaments and special structures of diarthrodial joints as well as the specific muscles involved in static and dynamic loading.

General program

The program generally consisted of invited key reviews on selected topics by leaders in the field (Table I), oral presentations selected from abstracts (Table II), including four awards given to young investigators (Fig. 2), and poster presentations selected from abstracts (Table III) which had been submitted for the workshop.

Imaging biomarkers and clinical outcomes in cartilage repair

The first review (Christoph Erggelet, University of Freiburg Medical Center Freiburg/Germany) focused upon the principles of surgical cartilage repair techniques and their applicability to OA, including early prevention, treatment of symptoms and cartilage changes, and replacement (arthroplasty). The presentation summarized repair techniques currently available and those being actively investigated, including clinical trials intro their effectiveness, and outlining current treatment options and their pros and cons with particular reference to lesion size[3].

Description of the imaging techniques and biomarkers for monitoring cartilage repair was then reviewed by Siegfried Trattnig (High Field MR Center, Medical University of Vienna, Austria). This included methods for assessing (1) glycosaminoglycan content [delayed gadolinium enhanced MRI of the cartilage (dGEMRIC),

Table I
Presenters and titles of invited presentations at the fifth Workshop on OA Imaging

Session 1:
Sample guiding question: what clinical outcomes should be used in cartilage repair and which imaging biomarkers predict these most effectively?

Christoph Erggelet, Educatis University, Altdorf, Switzerland
Surgical cartilage repair techniques and their applicability to OA

Siegfried Trattnig, Center of Excellence for High Field MR, Medical University of Vienna, Austria
Imaging techniques and biomarkers for monitoring cartilage repair

Stefan Marlovits, Medical University of Vienna, Austria
Clinical outcomes and their relationship with imaging biomarkers for cartilage repair

Session 2:
Sample guiding question: what have we learned from the OAI and where do we go?

Michael Nevitt and John Lynch, OAI Cooridinating Center, University of California, USA
Rates of structural OA progression (X-ray and MRI) in the OAI (and other epidemiological studies)

Kent Kwoh, University of Pittsburgh, USA
Relating structural OA progression (X-ray and MRI) to clinical outcomes in the OAI

Gayle Lester, NIH, USA
Current status, future perspectives and funding opportunities for the OAI and OA research

Session 3:
Sample guiding question: what clinical outcomes should be used in OA and which imaging biomarkers predict these most effectively?

Gillian Hawker, Women's College Hospital, University of Toronto, Canada
Clinical outcomes: what is the choice in OA?

Tuhina Neogi, Boston University, USA
Review of the relationship between X-ray biomarkers and clinical outcomes in OA

David Hunter, University of Sydney, Australia
Review of the relationship between MR imaging biomarkers and clinical outcomes in OA

Gloria Matthews, Genzyme Corp., Cambridge, USA
What requirements does an imaging biomarker need to satisfy to be useful in cartilage repair evaluation and DMOAD development?

Fig. 1. Participants of the fifth imaging workshop in OA in the courtyard of PMU, Salzburg, Austria.

Table II
Presenters and titles of oral presentations at the fifth Workshop on OA Imaging, selected from abstracts, including young investigator awards

Session 1: Cartilage Repair	
Frank Roemer Augsburg & Boston	Focal cartilage damage of the knee joint and risk for subsequent cartilage loss: an MRI-based analysis from the multi-center OA study (MOST)
Katarina Kulmala Kuopio	Contrast enhanced computed tomography in evaluation of spontaneous cartilage repair
Jasper Van Tiel Rotterdam	CT arthrography to measure cartilage quality: influence of sulfated glycosaminoglycan content and structural composition of extracellular matrix on contrast agent diffusion into cartilage
Jose Tamez Pena Monterrey	A quantitative method for evaluating cartilage defect repair: intra- and inter- reader reproducibility
Shive Matt Montreal	T2 MRI of repair cartilage reflects both tissue quality and quantity
Session 2: The OAI	
Richard Frobell Lund	MRI-based cartilage thickness loss and JSN in an OAI core progression sample, and their relationship with age, sex, and body mass index (BMI)
Jose Tamez Pena Monterrey	Spatio-temporal analysis of the significant changes in cartilage morphology: data from the OAI
Wolfgang Wirth Salzburg	Are short-term rates of MRI-based measures of knee cartilage loss markers of long-term change? 4-year data from the OA initiative
Eveliina Lammentausta Oulu	T2 reveals early cartilage changes during 2 years follow-up in subjects at risk for OA: data from the OAI
Robert Buck Minnesota	Correlation of knee cartilage thickness change at 1 year and clinical outcome changes at 3 years: data from the OAI
Session 3: Young investigator awards	
Claire Donoghue London	Automatically generated novel diagnostic imaging biomarkers with data from the OAI
Karen Wiegant Utrecht	Structural cartilage parameters on MRI and X-ray improve after treatment with knee joint distraction; a 2-year follow-up
Ida Haugen Oslo	MRI is more sensitive than conventional radiography in detection of erosions in hand OA
Laura Laslett Hobart	A 12-month randomized controlled trial of zoledronic acid for knee pain and subchondral BMLs
Session 4: Semi-quantitative imaging outcomes	
Dieuwke Schiphof Rotterdam	How risk factors associate to early OA shown with semi-quantitative measures on MRI in knees without signs of radiographic OA
Jos Runhaar Rotterdam	Malalignment and the presence of early signs of knee OA in obese women
Ali Guermazi Boston	Does MRI depict progression of radiographically-defined 'end-stage OA (KL grade 4)' longitudinally? The MOST study
Martin Englund, Lund and Boston	Risk factors for medial meniscal lesions and (OR) extrusion on knee MRI in older US adults: MOST
Kent Kwoh, Pittsburgh	Identification of MRI morphologic features associated with different knee pain patterns
Session 5: Quantitative imaging outcomes	
Michel Crema Boston	dGEMRIC and its relationship with medial meniscal pathology: a 12-month follow-up study using 3.0 T MRI.
Toshiyuki Shiomi Osaka	The influence of medial meniscectomy to the stress distribution of femoral cartilage in porcine knee – 3D reconstructed T2 mapping study
Satoru Tamura Osaka	Assessment of knee cartilage in patients with Anterior cruciate ligament (ACL) rupture by 3D reconstructed T2 mapping
Greg Cicconetti Philadelphia	Applying a statistical/graphical tool to characterize changes over time in MRI-based cartilage thickness measures
Robert Buck Minnesota	Simulations to assess behavior of ordered values approach in clinical drug trials

sodium imaging, chemical exchange saturation transfer (CEST)], (2) the collagen fiber network (global and zonal T2 mapping) and the diffusion properties of cartilage (diffusion weighted imaging)[4], including *in vivo* human studies performed at 7 T. Examples of application in different cartilage repair procedures were given and the need for the clinical validation of the biochemical (compositional) MR parameters was highlighted.

Clinical outcomes and their relationship with imaging biomarkers for cartilage repair were reviewed by Stephan Marlovits, Department of Orthopedics, Medical University of Vienna, Austria. Not unlike OA, symptoms in cartilage repair do not necessarily correlate with structural cartilage damage and/or structural improvement after repair. A key element is the application of "morphological" imaging, to allow for semi-quantitative scoring (e.g., the Magnetic Resonance Observation of Cartilage Repair Tissue (MOCART) score[5]), in order to assess the structural status of the repair. Additional applications in clinical studies include biochemical imaging and biomechanical MRI (how does the tissue function under movement and mechanical loading)[6].

Fig. 2. Young investigator award winners of the fifth imaging workshop in OA in the lecture theater of PMU, Salzburg, Austria (from left to right: Laura Laslett, Hobart; Karen Wiegant, Utrecht; Claire Donoghue, London; Ida Haugen, Oslo; Felix Eckstein) (chairmen of young investigator award session and local organizer).

The OAI

The OAI is currently and will continue to provide an unparalleled, state-of-the-art longitudinal public database of images and clinical outcome information to facilitate the discovery of biomarkers for development and progression of OA[7]. The workshop brought together experts in the field that helps to shape what questions might be prioritized to best utilize this vast imaging resource.

The first presentation by Michael Nevitt and John Lynch (Coordinating Center of the OAI, University of California, San Francisco), focused on new radiologic outcomes data from entral image assessments, including semi-quantitative and quantitative readings of fixed flexion knee radiographs, methods and results for determining progression, tips on using the data, and comparisons with MRI-measured cartilage thickness change. Rates of progression in OAI appear to be comparable to other observational studies [i.e., the summary measures from the OARSI Food and Drug Administration (FDA) initiative][8]. MRI appears to pick up higher number of progressors than radiography, and as radiographic OA becomes more severe [e.g., greater Kellgren–Lawrence (KL) or joint space narrowing (JSN) grades], MRI may become more responsive than radiographic measurement of joint space width (JSW).

Table III
Presenters and titles of poster presentations at the fifth Workshop on OA imaging

Lickorish D North Grafton	Quantification of trabecular bone vascularity in a rabbit model of OA by perfusion micro-computed tomography
Maschek S. Munich	Does ankle cartilage adapt to strong alterations in loading environment after transplantation to the knee (Van Nees rotationplasty)?
King. A.J. Calgary	3D visualization and measurement of the posterior cruciate ligament in a flexed knee using open-bore 0.2 T MRI
Dam E.B. Copenhagen	Automatic segmentation of bone and cartilage from knee MRI
Lammentausta E. Oulu	*In vivo* transport of GD-DTPA2 − into human knee cartilage
Eckstein F. Salzburg	Cartilage thickness, denuded areas, and bone size in knees prior to TKR − data from the OAI
Sitoci H. Munich	Nocturnal changes in femoro-tibial cartilage thickness in young healthy adults
Roemer F.W. Augsburg	Longitudinal within-grade scoring of cartilage and BMLs: validity analyses from the MOST study
Cicconetti G. Philadelphia	A statistical/graphical tool to identify knee OA phenotypes based on MRI cartilage thickness measures
Haugen I.K. Oslo	The role of MRI-defined synovitis in hand OA
Wyman B.T. Groton	Compression of the knee upon weight loading in healthy and OA subjects as measured by MRI and X-ray
Saunders F.R. Aberdeen	Active shape modeling of bilateral knee OA in the OAI
Driban J.B. Boston	Hip bone mineral density does not influence tibio-femoral BML size
Marques J. Copenhagen	Quantification of trabecular tibia bone structure related to the presence of OA
Marques J. Copenhagen	Prediction of cartilage loss by analysis of trabecular tibia bone structure
Riek J.K. New York	A multi-center comparison of T2 relaxation times calculated centrally vs those generated directly by the MR scanner
Beattie K.A. Hamilton	Longitudinal changes in intermuscular fat volume and quadriceps muscle volume in the thighs of female OAI participants
Rudolphi K. Frankfurt	Improved assessment by quantitative digital histomorphome-try of histopathological changes of articular cartilage in a surgical model of post-traumatic OA of the knee joint in rats
Stok K.S. Zürich	Comprehensive morphological characterization of arthritis in animal models by micro-computed tomography
Stok. K.S. Zürich	An intergrative imaging approach for examining bone and cartilage tissues in the osteoarthritic joint − a pilot study
Siorpaes K. Salzburg	Interobserver variation of quantitative meniscus analysis using coronal MPR DESSWE and IW TSE MR imaging
Blöcker K. Salzburg	Size and position of the healthy meniscus, and its correlation with sex, height, weight, bone size, and age
Kinds M.B. Utrecht	Are separate quantitative radiographic features (Knee Images Digital Analysis (KIDA)) of knee OA very early in the disease (check) associated with clinical progression during 4-year follow-up?
Kinds M.B. Utrecht	Feasibility of bone density evaluation using plain digital radiography
Hudelmaier M. Salzburg	1-year rate of change in subchondral bone size in osteoarthritic and healthy knees
Sattler M. Salzburg	Side differences of thigh muscle cross sectional areas in knees with the same radiographic OA (KL) grade, but unilateral frequent pain
Cromer M. Sydney	Quantitative analysis in the medial tibio-femoral compartment over 1 year
Nishii T. Osaka	Significant influence on load response of knee cartilage T2 by meniscus disorder − a loading MRI study
Noelle-Klocke N.F., Iowa City	Toward T1RHO in the clinic: a 3.0 T and 1.5 T comparison
Stannus O.P. Hobart	Cartilage signal intensity on MRI: association with BMI, cartilage defects and type II collagen break down
Buck R.J. Minneapolis	Classification and distribution of cartilage thickness change in subject knees: data from the OAI
Tummala S. Copenhagen	Diagnosis of OA by automatic quantification of incongruity from knee MRI
Tamura S. Osaka	3D patterns of acetabular cartilage damage in hip dysplasia at pre- and early arthritic stages; a high-resolutional CT arthrography study
Lowitz T. Nürnberg	Quantitative CT for knee OA

The inter-rim distance appears to have a large effect on the direction of quantitative JSW change and its intersubject variability, with change in tibial rim distance serving as a surrogate for change in alignment of the tibial plateau relative to the X-ray beam. Adjusting for this effect may improve JSW as an outcome; however there appears to be additional need to develop methods for dealing with non-ideal radiographs for JSW measurement changes.

Kent Kwoh (University of Pittsburgh) summarized emerging data on the relationship of bone marrow lesions (BMLs), effusion, synovitis, and denuded bone areas (dABs) with pain in the OAI, as a function of score/size and location. New opportunities have emerged within the OAI to relate these and other morphological features to total knee replacement (TKR). Thus far (from baseline through to the 72-month follow-up visit) 254 TKRs have reported in the OAI, 18 with a baseline KL grade of 0 or 1, 54 with 2, 98 with 3, and 84 with a KL grade of 4. New data is emerging indicating that MRI cartilage morphometry [denuded bone areas (dAB) and cartilage thickness] as well as a range of clinical variables (pain and function) predicts the advent of TKR.

Finally, Gayle Lester [National Institute of Health (NIH)] summarized the current status, future perspectives and funding opportunities for the OAI[9]. She pointed out that the OAI is now funded for a total of 8 years of follow-up, with the 60-month visits almost completed, the 72-month visits approximately 70% completed, and the 84-month visit started in February 2011. Retention remains high with follow-up in the study of about 80% of the original cohort. The OAI contract ends in 2014/2015, and the goal is to transition to grants for follow-up analyses. She encouraged more studies using OAI and ancillary studies, potentially introducing novel imaging methods within the last 2 years of the study.

Relationships of imaging biomarkers with clinical outcomes

OA is extraordinarily complex with marked heterogeneity in onset, clinical presentation, rate of disease progression, pattern of joint involvement and different tissue structures being affected. An important challenge is that the current approval of potential disease modifying OA drugs (DMOADs) requires structural alteration to be linked to a clinical benefit, either at the same time of structural measurement or later. With this in mind it is important that improvements in OA structural features are related to symptoms, function, or joint survival, i.e., time to (need for) TKR.

As presented by Gillian Hawker (University of Toronto, Canada), the current clinical focus is on pain, as this is the predominant reason a patient will seek clinical care. However, there are many downstream effects of pain, including fatigue, depressed mood and disability, which amplify pain and its experience over time. These should not be forgotten in the assessment of OA, with a need for a broader bio-psycho-social perspective[10]. Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) pain scores appear to largely reflect pain occurring with activity, and the correlation with function subscales is high: therefore WOMAC scores are apparently insufficient, if one is interested in pain and disability as separate constructs. The OARSI–Outcome Measures in Rheumatoid Arthritis Clinical Trials (OMERACT) working group identified distinct types of OA pain, one being a dull, aching pain, which became more

constant over time, and the other one an episodic type of pain that is generally more intense, often unpredictable, and emotionally draining. Intermittent, intense, unpredictable pain has the greatest impact on quality of life. New subscales are being developed that account for differences in types of pain and that are independent of joint function. An OMERACT–OARSI working group found that patients with an indication to TKR had greater pain and disability than those without, but due to considerable overlap in the scores the group was unable to determine relevant cut-points, so that a concept of virtual TKR is still under development[11].

As outlined by Gloria Matthews (Genzyme Corporation, Cambridge, MA), the guidance and current gold standard for measuring clinical efficacy of DMOADs is radiographic JSN or change in JSW[12], from which the integrity and thickness of articular cartilage (and the meniscus) are inferred[13,14]. The current guidance describes a process of drug approval for specific indications in OA, e.g., treatment of symptoms, delays in structural progression, and even prevention. JSN is currently recommended as an imaging endpoint for clinical trials on DMOADs by both the FDA and the European Agency for the Evaluation of Medicinal Products (EMEA) and ideally should be paralleled by symptom evidence. Alternatively, plans for assessing long-term clinical outcomes should be discussed with the agencies. At present, alterations in structural progression need to be determined by radiography, but MRI is now also recommended for clinical trials by the agencies for cartilage morphology (volume/thickness) assessment. It is possible that newer technologies may be approved in the future, including biochemical markers, MRI or even ultrasound, once appropriately validated[15,16]. However, minimum clinically important differences need to be established and the durability of the effect demonstrated. The FDA guidance is currently under review with efforts from an OARSI led initiative[17]. With regard to the evaluation of cartilage repair procedures, MRI may serve as a co-primary or secondary endpoint, with pain and function being primary endpoints. The MRI techniques applied need to be clearly defined in the study protocol and images should be evaluated by at least two independent (blinded) readers. The protocol should include prospectively stated descriptions of the image review process, including a plan for resolving conflicting readings. In contrast to the FDA, the EMA recommends second look arthroscopy, ranking histological evaluation higher than MRI.

As outlined by Tuhina Neogi (Boston University, Boston, MA), X-ray changes of OA typically take a long time; incidence rates of knee OA are about 6% over 30–36 months. Difficulties in studying relevant clinical OA outcomes in epidemiologic studies arise from the fact that all clinical outcomes are influenced by factors other than OA itself. Further, pain is subjective, function is a person-level concept, whereas OA is a joint-level phenomenon, and TKR depends upon factors other than disease, pain or function. Therefore, at present, KL grade or JSW cannot accurately predict TKR with appropriate specificity, neither when analyzed cross-sectionally nor longitudinally. Although the relationship between radiographic change and clinical outcomes is often described as weak, this is potentially due to between-person confounding. Novel analytic techniques (between-knee, within-person comparisons) are finding stronger associations[18] and these are consistent across different racial/ethnic groups. These studies show that JSN is more strongly associated with pain than osteophyte scores. Ideally, pain should be assessed more frequently than is currently feasible in most observational studies, to more accurately capture pain fluctuations. It is stressed that alterations in some structural lesions may result in short-term clinical outcome effects, but for others, any potential effect may be detected only with longer follow-up.

David Hunter (University of Sydney, Sydney Australia) reviewed the relationship between MRI biomarkers and clinical outcomes in OA. MRI measures [especially synovitis, effusion, BMLs, denuded areas of bone (dABs)] provide a stronger relation to symptoms than other structural changes[19]. There are a number of complex hurdles with regards validating and qualifying MRI biomarkers that need to be overcome, to utilize these measures in clinical trials and gain regulatory assent as an approved endpoint.

Round table discussion and new directions

The conference closed with a vigorous discussion on "How can we clinically validate and qualify existing imaging biomarkers for cartilage repair and OA?" As part of this discussion a number of new initiatives and propositions were discussed that could help to overcome some of the obstacles in the field.

One proposal was to not view structural (radiographic) OA as a disease, as long as it represents an asymptomatic condition. However, structural OA may be considered a "risk factor" of the disease (i.e., symptomatic OA). A DMOAD thus should not be necessarily expected to have an immediate or short-term effect on clinical outcomes (i.e., symptoms and function), but may reduce the risk of disease onset or disease progression over longer periods. In that sense, DMOAD treatment may be equivalent to treatment of high blood pressure, high lipid or high glucose serum levels in context of stroke, coronary heart disease, or diabetes. Prospective, observational studies are needed showing to what extent structural imaging biomarkers can predict clinical outcomes years later. However, some of the most promising novel imaging biomarkers also will have to be tested in parallel with radiography in initial therapeutic (DMOAD) trials, in order to demonstrate their usefulness to regulatory agencies.

The STAIR – Stroke Treatment Academic Industry Round table – Consensus Conferences potentially provide a useful model for the OA field[20]. These are intended to improve the understanding of issues critical to stroke drug and device development and advance knowledge essential to the successful development of new acute stroke treatments. STAIR assembles a select group of leading scientists from industry, academia and government (including FDA) to initiate a consensus process that results in the development of recommendations, and from which a manuscript is submitted to a leading medical journal.

Foundation for National Institutes of Health (fNIH) OA biomarkers consortium

It is evident that new investigational paradigms in drug development must be advanced to facilitate both discovery and clinical development, without sacrificing basic regulatory standards of safety and efficacy[21]. Cognizant of these challenges, there is evidence that the stakeholders in the pharmaceutical enterprise recognize the need for a shift in the approach to drug development[22,23].

The Biomarkers Consortium is a public–private partnership managed by the FNIH (http://www.FNIH.org) with broad participation from many private, academic, and non-profit stakeholders. It endeavors to identify, develop, and qualify biological markers (biomarkers) to support new drug development, preventive medicine, and medical diagnostics[21,24]. An OA Biomarkers Consortium has recently formed under the organizational umbrella of the fNIH[25]. The hope is that through this mechanism an approach to clinical validation and qualification of high potential OA biomarkers will be facilitated providing the most effective means to driving breakthroughs leading to viable new chemical entities for patients with OA.

Next meeting

The next workshop will be a joint workshop (sixth OA imaging workshop in combination with the OARSI OA Biomarker Workshop

III) and will take place at Hilton Head (South Carolina) from July 12th to 14th 2012. The highlights and focus of the meeting will be:

1. A pre-course on the practical use of imaging biomarkers in clinical studies/ trials.
2. Discussion of the pathway for validation and qualification of OA biomarkers.
3. Discussion of the level of validation/ qualification key efficacy of intervention biomarkers.
4. Discussion of the steps needed to overcome obstacles and improve biomarker qualification.

Author contributions

- Conception and design (all authors)
- Analysis and interpretation of the data (all authors)
- Drafting of the article (all authors)
- Critical revision of the article for important intellectual content (all authors)
- Final approval of the article (all authors).

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