Methods:

To provide an introduction to Immunohistochemistry and
McGill Univ. Imaging Facility, Montreal, QC, Canada

C.M. Brown

IMMUNOHISTOCHEMISTRY AND CONFOCAL TECHNIQUES

V. Byers-Kraus
Duke Univ., Durham, NC

Purpose: Evaluating the clinical effectiveness of drugs for OA
poses special challenges because of the difficulty in assessing the
stage and state of the disease, the slow changes in the current
radiographic measure of joint space narrowing, and the duration of
the studies necessary to show significant effects. Biomarkers are
potential means of providing quantitative and objective indices
to help overcome some of these challenges.

Methods: Before a biomarker is eventually adopted as a clinical
tool, it requires biological and clinical validation, ideally in large
numbers of patient samples. The evidentiary process linking a
biomarker with biology and clinical end points has recently been
defined as biomarker qualification.

Results: Although the qualification of OA biomarkers is gaining
momentum, the current state of biomarkers for OA is analogous
to the state of biomarkers for osteoporosis 30 years ago. Unlike
osteoarthritis, for which bone density emerged as the gold standard
measure, in OA it remains to be determined what surveillance
measures will ultimately be adopted. Like osteoporosis, OA has a
silent molecular stage, and late stage adverse outcomes. OA has
added complexity and heterogeneity with different patterns of joint
involvement and different inciting pathologies including genetics,
injury, and joint anatomy to name a few.

Conclusions: Increasingly, studies are demonstrating biomarkers
with the ability to quantify various dimensions of the OA process
with accuracy and precision. Biomarkers used singly and in com-
bination, in conjunction with imaging, demographics, and OA risk
factors, provide a rich toolset for evaluating the efficacy of drugs
for OA. Increasing use and reliance on a comprehensive toolset, it
is hoped, will contribute substantially to development and approval
of therapeutics to favorably impact the course of this disease.

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IMMUNOHISTOCHEMISTRY AND CONFOCAL TECHNIQUES

C.M. Brown
McGill Univ. Imaging Facility, Montreal, QC, Canada

Purpose: To provide an introduction to Immunohistochemistry and
Confocal Imaging Techniques

Methods: How to perform imaging of immunohistochemistry sam-
plies either with a colour camera or blue, green and red filter sets.
How to generate high quality confocal images and to separate
fluorescence dyes with similar fluorescence spectra. How to re-
move specimen auto-fluorescence from the signal from specific
fluorescence probes.

Results: Proper camera colour balance is required to gener-
ate suitable images of immunohistological samples. Three im-
ages using blue, green and red filters can be generated using a
monochrome camera and overlayed in image processing software
in order to image Immunohistological samples without the need
for a colour camera. With the proper imaging settings high qual-
ity confocal images can be generated from fluorescent samples.

Spectral imaging can be used to separate dyes of similar colour
and to remove specimen auto-fluorescence.

Conclusions: Following this presentation attendees should have
a clear idea of the main aspects to keep in mind when performing
brightfield or confocal imaging.

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STRATEGIES TO USE MODERN IMAGING TECHNOLOGIES
TO EVALUATE PATIENTS WITH OA

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Purpose: The radiographic examination of joints is useful in the di-
agnosis of osteoarthritis (OA) and has enabled significant progress
to be made in our understanding of risk factors for OA. However
new imaging modalities provide novel opportunities to investigate
the pathogenesis of OA through examining the whole joint. The
aim of this presentation is to examine current strategies using
modern imaging technologies in the evaluation of patients with OA
and to consider the potential impact of these new approaches.

OA is a disease of the whole joint. By using improved, non-invasive
techniques such as magnetic resonance imaging (MRI) to visu-
alis the whole joint, it is now possible to examine the relative
role of different joint structures such as cartilage, bone, menisci,
synovium and ligaments simultaneously on the symptomatology
and progression of OA. Recent work demonstrates that knee OA is
the result of multiple, cumulative changes in joint structure occur-
ing in the apparently healthy, asymptomatic state, which progress
until clinical disease presents itself. The use of MRI, a sensitive
and non-invasive tool, has enabled the examination of these early
changes of OA, prior to radiographic disease, through to the joint
with end stage disease. This shows that our current definitions of
radiographic tibiomeral OA fail on the continuum from health to
disease, with approximately 10% of articular knee cartilage lost
before radiological disease is detected. Since OA is recognised
as a multifactorial disease, using a sensitive examination of joint
structure, provides opportunities to examine new hypotheses in
the pathogenesis of OA. Identifying early changes may provide
novel targets for the prevention and treatment of knee OA. At
an individual level, they may also help identify those at risk of
OA who may benefit from early lifestyle modification. Although
much of the current work has focussed on MRI, other modalities
such as ultrasound, scintigraphy, and CT are also being used in
the evaluation of patients with OA and provide complementary
information.

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NEW APPROACHES TO MEASUREMENT OF OUTCOMES
TO ASSESS EFFICACY OF OSTEOARTHRITIS TREATMENT:
The OARSI-OMERACT INITIATIVE

M. Dougados
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Purpose: In order to propose a set of criteria for considering
total articular replacement (e.g. medical treatment failure) to be
used as an end-point in clinical trials evaluating potential disease
modifying drugs, a joint OARSI-OMERACT initiative is aiming at