Rheumascal - A new method for assessment of rheumatoid arthritis in finger and hand joints: Procedure details

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Learning objectives

In this educational exhibit, we elucidate the Rheumascan procedure. It is a new method using contrast enhanced optical imaging with a dedicated imaging system, the Xiralite system. Procedure details as well as the pathophysiological backgroung for fluorescence imaging in inflammation are given.

Background

Imaging of microcirculation with fluorescence optical imaging

Contrast-enhanced optical procedures are established worldwide for imaging of small and smallest vessels. Most common is fundus angiography with Fluorescein or ICG as fluorophor. Besides imaging of small vessels as directly visible structures the more two-dimensional aspect of contrast enhancement caused by the microcirculation is integral part of the exam. Regionally less perfused areas are visible as focal inhomogeneities of contrast enhancement(1).

Imaging of microcirculation with ICG is well established in plastic and reconstructive surgery. The postoperative microvascular perfusion of transplanted vascularized flaps has been examined. In a study with 15 patients, Lamby et al.(2) analyzed the use of ICG as well as other imaging modalities for imaging of microvascular perfusion of vascular parascapular flaps transplanted to the forefoot. ICG allowed verifying microvascular perfusion of the transplanted flaps.

Diseases leading to disturbance of microcirculation can be diagnosed with fluorescence based optical imaging, e.g. in patients with tumors of the eye. Schaller et al.(3) studied 13 patients with choroidal melanomas before and for one year after brachytherapy, using ICG-based fluorescence imaging. Microcirculation of the tumors was visualized. In 10 of the 13 patients, the microvascular effects of brachytherapy were seen, causing a reduction of visible microvascular vessels.

In a prospective study, Mueller et al.(4) studied the potential of ICG-based imaging of the microcirculation in the eye. Overall, 98 patients with small choroidal melanomas were classified using a variety of different parameters. Microcirculation parameters, collected with ICG-based optical imaging, had the strongest association with the time of prospective defined tumor growth. Thus, depiction of clinically relevant changes in microcirculation patterns gives relevant clinical information.

Overall, ICG-based fluorescence optical imaging is well suited to delineate changes of the microcirculation throughout a variety of different clinical entities.
Fluorescence imaging of rheumatoid arthritis

Pathophysiology

The true cause of rheumatoid arthritis remains unclear despite intense research. Varieties of immune cells are activated during active disease and secrete proinflammatory cytokines, interleukins, and other factors. These mediators promote the inflammation and result in a destruction of the adjacent synovial structures. In addition, neoangiogenesis is triggered in the region of the synovial membrane(5). This however leads to synovial contrast enhancement in contrast-enhanced ultrasound as well as contrast-enhanced MRI(6). Due to the direct visualization of increased blood supply to the tissue during disease activity, both methods are in principle superior to other clinical and imaging tests, which do not show this early pathophysiologic process of inflammation(7). On this basis it is clear, that an appropriate imaging test is superior to currently established clinical procedures.

Experimental evidence

Fluorescence optical imaging is capable of delineating microvascular changes in humans, and microvascular alterations are an integral part of active inflammatory processes. Fischer et al.(8) were able to demonstrate the potential of direct fluorescence optical imaging of inflamed joints. In a study with induced Lyme-arthritis in mice (n=20) and 20 healthy control animals, optical imaging was performed with an excitation wavelength of 740 nm, fluorescence signals were detected above 800 nm. The tested fluorescence dyes were able to differentiate affected from non-affected joints.

Imaging findings OR Procedure details

The Xiralite system is dedicated for simultaneous imaging of all joints in both hands. It uses dark red and near infrared light in combination with the fluorescence dye indocyanine green (ICG). It utilizes the increased vascularity and blood flow in active inflammatory processes. Digital image handling is integrated.

After establishing an i.v. access, the patient places his hands on a preformed hand rest. The Rheumascan is started and ICG is injected intravenously (0.1mg/kgBW). During the procedure, fluorescence intensity (> 800 nm) is acquired every second for 6 minutes over both hands. At the end of the procedure, images are displayed as an image stack, and represent the dynamics of the contrast distribution over time.
After placement of both hands in a preformed handrest, image acquisition is started. The fluorescence distribution is measured for 6 minutes. Evaluation of the image stack takes approximately 2 to 5 minutes. Overall, the procedure takes less than 15 minutes.

References: mivenion GmbH, Berlin, Germany

The whole workflow of the procedure is displayed in Fig. 1.

Xiralite uses dark red light for excitation of ICG fluorescence. The patient can sit relaxed during the exam.

When evaluating the imaging findings, first the image with maximum intensity is selected and the image stack is window/level adjusted to this image. The assessment of findings than is done in scrolling through the image stack, looking for joint-associated differences.
in signal intensity. While using the scrolling mode, anatomical enhancement, e.g. in veins, is easily depicted.

Software is available to normalize the fluorescence signals to the unaffected finger tips. The normalized image stack can than be displayed as a single image representing the area-under-curve (AUC) of the whole procedure. AUC images are displayed in poster C-2255 at the ECR 2010.

On the basis of normalized AUC - images, a quantitative follow-up of treatment effects can be measured.

<table>
<thead>
<tr>
<th>Joint</th>
<th>Visual Scoring</th>
<th>Change of SI-AUC (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>L-PIP3</td>
<td>-</td>
<td>-27</td>
</tr>
<tr>
<td>L-PIP2</td>
<td>-</td>
<td>-29</td>
</tr>
<tr>
<td>L-wrist</td>
<td>-</td>
<td>-55</td>
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<tr>
<td>R-PIP3</td>
<td>+</td>
<td>-17</td>
</tr>
<tr>
<td>R-wrist</td>
<td>+</td>
<td>-51</td>
</tr>
</tbody>
</table>

Mean inhibition of inflammation of 35.8% by Doxycycline within 10 weeks treatment

**Fig.**: Follow-up of a patient with lyme - arthritis. The patient recieved treatment with doxycycline. Mean inhibition of inflammation was calculated at 36%.

**References:** Dr. Langer, Duesseldorf, Germany and mivenion GmbH, Berlin, Germany

**Images for this section:**

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**Fig. 1:** Schematic workflow of the Xiralite procedure. ICG is injected intravenously 10 seconds after start of image acquisition.
Conclusion

The Rheumascan procedure is easy to perform and takes less than 15 minutes for the complete, conclusive assessment of inflammation in all joints of both hands. With a standardized acquisition and evaluation procedure, assessment of disease activity in rheumatoid arthritis and other inflammatory diseases of the fingers and the wrist of both hands is fast and time efficient. Software algorithms allow normalization of signal intensities. Calculation of individual therapy response is possible on the basis of consecutive, normalized image sets.

Clinical cases are demonstrated in poster C-2255 at ECR 2010.

Images for this section:
Fig. 1: Schematic workflow of the Xiralite procedure. ICG is injected intravenously 10 seconds after start of image acquisition.
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