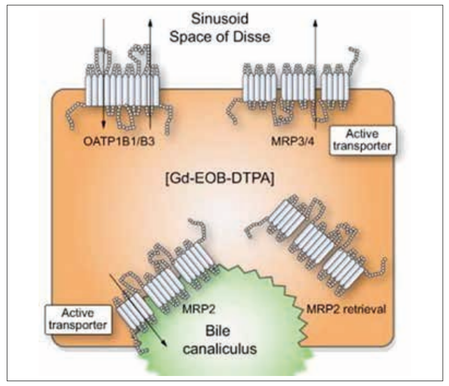
BY SABINE SCHMIDT KOBBE

Perfusion quantification and hepatic function with Gd-EOB-DTPA: hepatic fibrosis and hepatocellular transport



Schematic demonstration of the different membranous hepatocyte transporters responsible for the intracellular Gd-EOB-DTPA uptake and biliary excretion.

Assessment of liver perfusion and hepatic function is gaining importance, since surgeons increasingly resect larger volumes while the hepatic parenchyma may be altered by previous treatments and/or underlying cirrhosis. Consequently, postoperative liver failure may occur making the preoperative assessment of liver function mandatory. Liver biopsy remains the reference standard, but non-invasive imaging techniques are increasingly being developed. Several MR techniques of estimating liver function have been reported, including elastography, T1-relaxometry and techniques of signal-intensity measurements using the hepatospecific contrast agent Gd-EOB-DTPA. However, MR signal-intensity measurements need to be considered with caution, since they are not absolute values and no linear straightforward relationship with the contrast agent concentration exists. Therefore, pharmacokinetic modelling with Gd-EOB-DTPA seems a more appropriate method for quantifying hepatic perfusion and assessing liver function.

In the functioning hepatocyte, the uptake and intracellular concentration of Gd-EOB-DTPA depends on the activity of different membranous transporter proteins. The contrast agent enters via OATP2/8, exits through MRP2, while the transporters MRP3 and MRP4 allow the efflux back to the sinusoids (see figure). In healthy livers, Gd-EOB-DTPA is not metabolised inside the hepatocytes and is extracted unchanged into the bile. In diffuse liver disease, however, such as cirrhosis, the hepatocyte Gd-EOB-DTPA uptake and biliary excretion progressively decrease. The exact reason for this lesser contrast agent metabolism has not been elucidated yet, but it could result from lesser tissular expression of the hepatocyte transporters.

Therefore, we quantified hepatic perfusion and hepatocyte function by means of dynamic Gd-EOB-DTPA MRI and correlated our MR-findings with the immunohistochemical expression of the hepatocyte transporters. We prospectively investigated 42 patients with different stages of liver fibrosis who underwent dynamic Gd-EOB-DTPA-enhanced MRI (3T, 3D T1-w sequences) and liver biopsy.

Applying a dual-input tri-compartment uptake-excretion model we extracted various MR-perfusion parameters, such as arterial and portal perfusion, Gd-EOB-DTPA hepatocytic uptake rate, biliary efflux, sinusoidal back flux, and extracellular volume. Two pathologists classified the fibrosis according to METAVIR. The expression of the hepatocyte transporters was investigated by immunohistochemistry and semi-quantitatively scored according to their lobular distribution.

Our pharmacokinetic modelling enabled not only the quantification of hepatic perfusion, but also the evaluation of the hepatic function, since we could distinguish the different stages of fibrosis ($p<0.01$). At MRI, increasing fibrosis was associated with progressive change from portal to arterial perfusion, a decrease in hepatocytic Gd-EOB-DTPA uptake rate, biliary efflux, sinusoidal back flux, and increased extracellular volume ($p<0.05$). The hepatocyte uptake fraction had better diagnostic performance than the semi-quantitative hepatobiliary enhancement parameter for staging liver fibrosis.

At immunohistochemistry, increasing fibrosis was associated with a more diffuse expression of OATP2/8 and MRP3 to the whole lobule and progressively irregular MRP2 expression ($p<0.05$). Surprisingly, the expression of the hepatocyte transporters remained despite progressive fibrosis.

We conclude, therefore, that at advanced stages of liver fibrosis, the decrease in Gd-EOB-DTPA hepatocytic uptake may reflect either lower interstitial bioavailability of the contrast agent or any altered hepatocyte transporter functions. The modified immunohistochemical expression of the transporters could mean an adaptive response to progressive intracellular cholestasis.

Dr. Sabine Schmidt Kobbe is consultant radiologist at the University Hospital of Lausanne, Switzerland. She is one of three heads of abdominal imaging and her main interest is in hepatobiliary cross-sectional imaging, such as CT and MRI, in particular functional imaging (perfusion and diffusion).

Scientific Session: Abdominal Viscera

Wednesday, February 28, 10:30–12:00, Room B

SS 201a Multiparametric liver imaging

Moderators: A. Filippone; Chieti/IT
S. Ichikawa; Chuo-shi, Yamanashi/JP

» **Keynote Lecture**
D. Regge; Turin/IT

» **Perfusion quantification and hepatic function with Gd-EOB-DTPA: hepatic fibrosis and hepatocellular transport**
S. Schmidt[1], J.-L. Daire[2], A. Sciarra[1], B. Leporq[3], B. Van Beers[2], C. Sempoux[1], C. Pastor[4]; [1]Lausanne/CH, [2]Clichy/FR, [3]Villeurbanne/FR, [4]Geneva/CH

BY STEVE EBDON-JACKSON

Euratom Basic Safety Standards Directive: a comprehensive approach for radiation protection

The latest Euratom Basic Safety Standards Directive (BSSD) – 2013/59/Euratom – came into force on February 6, 2018. It replaces the previous BSSD from 1996, but also a range of other directives including the Medical Exposure Directive 97/43/Euratom. In doing so, the latest BSSD provides a comprehensive approach to radiation protection based on the latest thinking and evidence of radiation effects. The directive is intended to protect the public, workers and patients who are vulnerable to the dangers from ionising radiation exposure. This is particularly important for radiology services as well as other clinical departments that use ionising radiation for diagnosis, treatment or research.

The BSSD requires a comprehensive approach to notification, registration and licensing of practices including those in the clinical setting. The directive requires a graded approach with increasingly stringent controls related to the potential hazard and risks of the practice. An excellent example of this approach is the licensing required for the production, medical use and disposal of radioactive material used for molecular imaging in medicine. This epitomises the approach of the BSSD and addresses radiation protection of the public, workers and patients. Specific requirements about the medical use are included within Chapter VII of the directive, which deals with individual medical exposures.

The BSSD has always focussed on the radiation protection of workers. The latest BSSD demonstrates this directly by introducing new dose limits for the lens of the eye. Limits of 20mSv in a single year or 100mSv in any five consecutive years (subject to a maximum value of 50mSv in a single year) will be required in national legislation. These limits provide challenges for interventional radiology but are achievable if appropriate protection is used.

The new directive will also require that occupational and public exposures are considered when new types of radiological practices are being justified. Previously, the focus would have been on patient exposure alone. This approach recognises the importance of addressing radiation protection in a comprehensive manner.

For medical exposures, the BSSD introduces a range of new requirements intended to benefit patient radiation protection throughout the planning and delivery of care. The BSSD enhances previous requirements for justification and optimisation of medical exposures and the processes that support these. The requirements for clinical audit have not changed, but it is expected that they will become a focus for regulators in the next few years. Clinical audit, including aspects relating to radiation protection, has the potential to demonstrate improvements in patient safety and healthcare delivery through professional initiatives.

New requirements relating to equipment will ensure that information about an exposure is provided and available during and after the exposure, taking advantage of facilities that are available on the latest diagnostic equipment. Patients or their representatives are now required to receive information about the benefits and risks relating to the radiation dose from their procedures prior to the procedures taking place. If this is done sensitively and in the appropriate clinical context, this can only help to improve patients' confidence in radiology services and all the professionals that provide them.

In general, radiology services are among the safest delivered in healthcare, but occasionally things do not always go as planned and accidental and unintended exposures happen. In most cases there will be no clinically significant impact on the individual patient, but nevertheless it is important to ensure that the probability and magnitude of such exposures are reduced as much as possible. This directive requires clinicians to analyse and record all events or potential events of this nature which can improve the safety culture within departments and hospitals. If exposures are clinically significant, then information should be given to the patient or their representative and to the healthcare team looking after the patient. In some cases, defined by radiation protection authorities, significant, accidental or unintended exposures should be reported externally. This information can help prevent similar events on a national and international scale.

In summary, the latest BSSD provides an opportunity for European Union Member States to improve radiation safety for all those that may be exposed by introducing new national legislation and administrative processes. This opportunity is particularly welcome in the medical field.

Today, ECR 2018 features the EuroSafe Imaging session 'Euratom Basic Safety Standards Directive: a comprehensive approach for radiation protection' at 16:00 in Room M1. The session will provide an overview of the BSSD and provide the perspectives of regulators, industry and the European Commission. The session will conclude with a panel discussion on whether the Basic Safety Standards Directive is a step forward for patients, clinical professionals and regulators.

Steve Ebdon-Jackson works for Public Health England, having worked previously as a medical physicist in healthcare settings and as a policy maker and regulator for medical exposures within the government. He led the UK negotiations of the medical sections of the BSSD and has been instrumental in their transposition into UK law. He has served as the chair of the EC Article 31 Group of Experts Medical Exposure Working Party and the HERCA Working Group on Medical Applications. He is also active in WHO and IAEA initiatives.

EuroSafe Imaging Session

Wednesday, February 28, 16:00–17:30, Room M 1

EU 1 Euratom Basic Safety Standards Directive: a comprehensive approach for radiation protection

Chairpersons: G. Frija; Paris/FR
S. Ebdon-Jackson; Didcot/UK

» **Chairperson's introduction**
S. Ebdon-Jackson; Didcot/UK

» **The technical approach: achievements and future of dose reduction**
W.A. Kalender; Erlangen/DE

» **The clinical approach: the gap to be closed**
G. Frija; Paris/FR

» **The clinical audit: the missing link**
E.J. Adam; London/UK

» **The regulatory approach**
S. Ebdon-Jackson; Didcot/UK

» **The European Commission's perspective and update on the transposition in the European Member States**
G. Simeonov; Luxembourg/LU

» **The industry's perspective and work needed to comply with the Basic Safety Standards**
N. Denjoy; Brussels/BE

» **Panel discussion: Is the Basic Safety Standards Directive a step forward for patients, clinical professionals and regulators?**
G. Frija; Paris/FR

» **S. Ebdon-Jackson; Didcot/UK**
W.A. Kalender; Erlangen/DE

» **E.J. Adam; London/UK**
N. Denjoy; Brussels/BE
G. Simeonov; Luxembourg/LU

This session is part of the EuroSafe Imaging campaign.