

Hepatocyte Transporter Network 2019

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Bile acid tracer to analyse enterohepatic circulation by PET

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Enterohepatic circulation and bile acid transport

6–10 times/day in humans

Liver → Bile ducts

Portal venous circulation

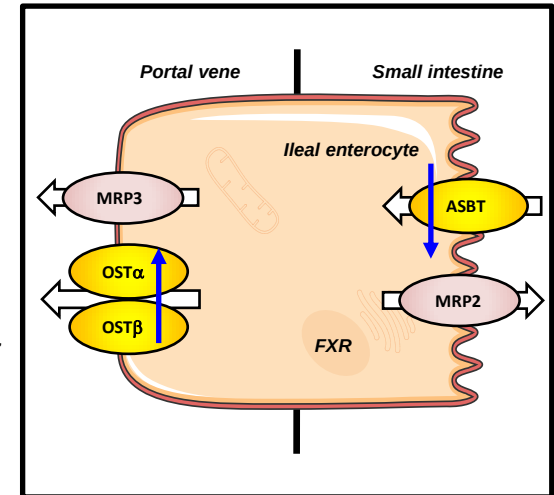
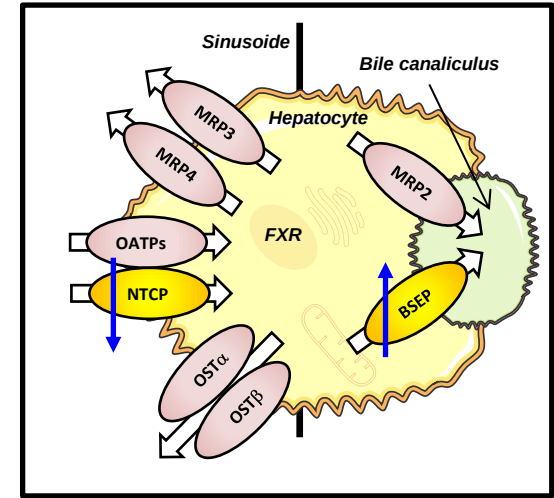
Small intestine (and gallbladder)

Terminal ileum

Colon (<5%)

Major bile acid transporter
Secondary bile acid transporter

Effect of bile acid-FXR on main transporters

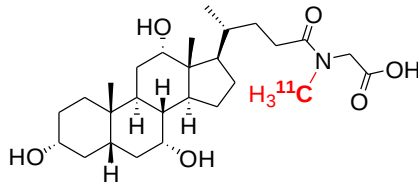


¹ Frisch & Hofmann. Biliary secretion. In: Functional Molecular Imaging in Hepatology, 2012, pp. 49-75

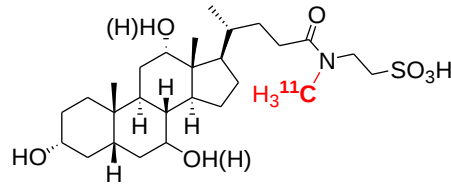
² Frisch & Alstrup. Physiol Biochem Zool 2018;91:797

PET-tracers to study bile acid transport

Next talk



***N*-[¹¹C]methyl-cholyglycine
([¹¹C]cholylsarcosine)^{1,2}**

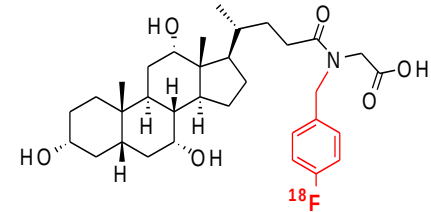


***N*-[¹¹C]methyl taurine
conjugated bile acids³**

Radioactive half-life: 20.4 min

(too short for studies of the enterohepatic circulation)

This talk



***N*-(4-[¹⁸F]fluorobenzyl)-cholyglycine
([¹⁸F]FBCGly)⁴**

Radioactive half-life: 109.8 min

¹ Frisch et al. *J Nucl Med* 2012;53:772

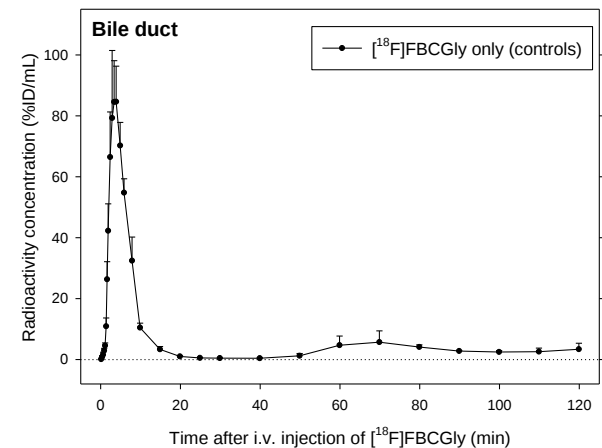
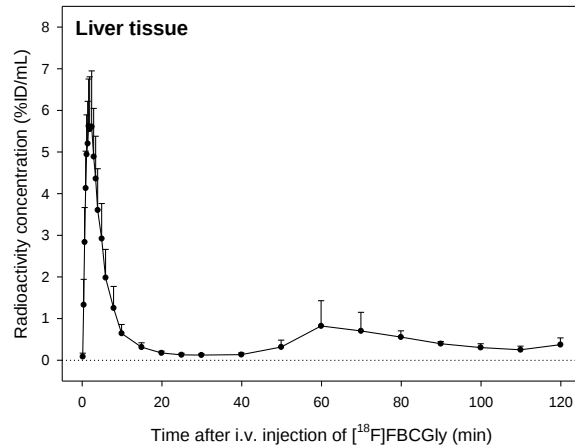
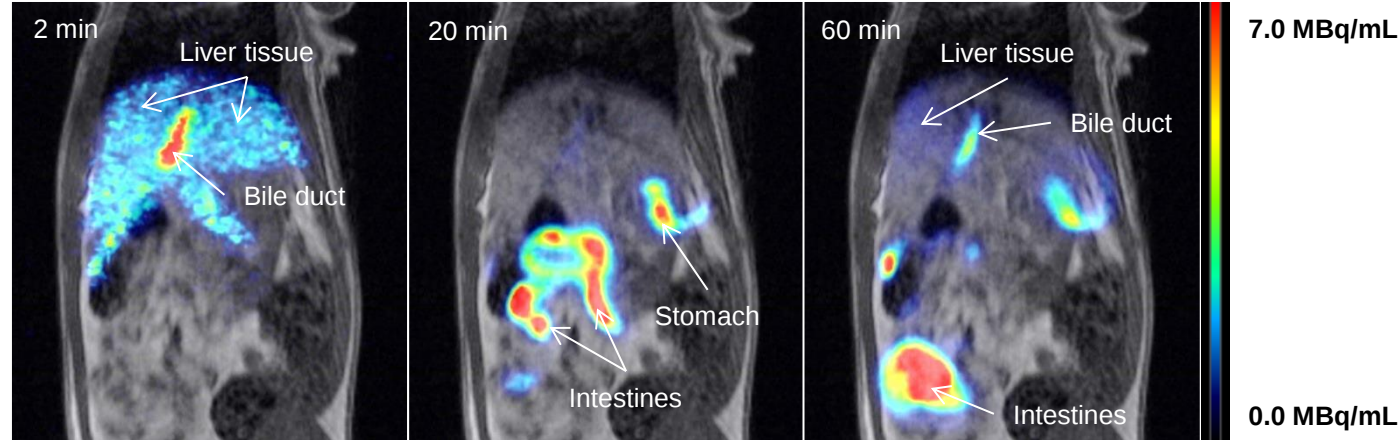
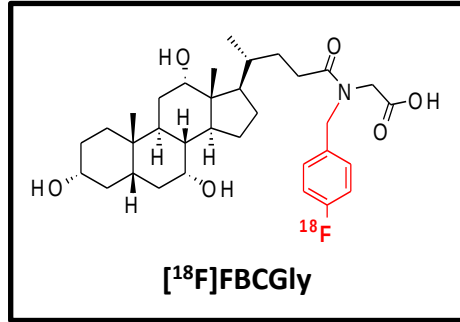
² Frisch et al. *Nucl Med Biol* 2019;72–73:55

³ Schacht et al. *J Nucl Med* 2016;57:628

⁴ Frisch et al. *Nucl Med Biol* 2018;61:56

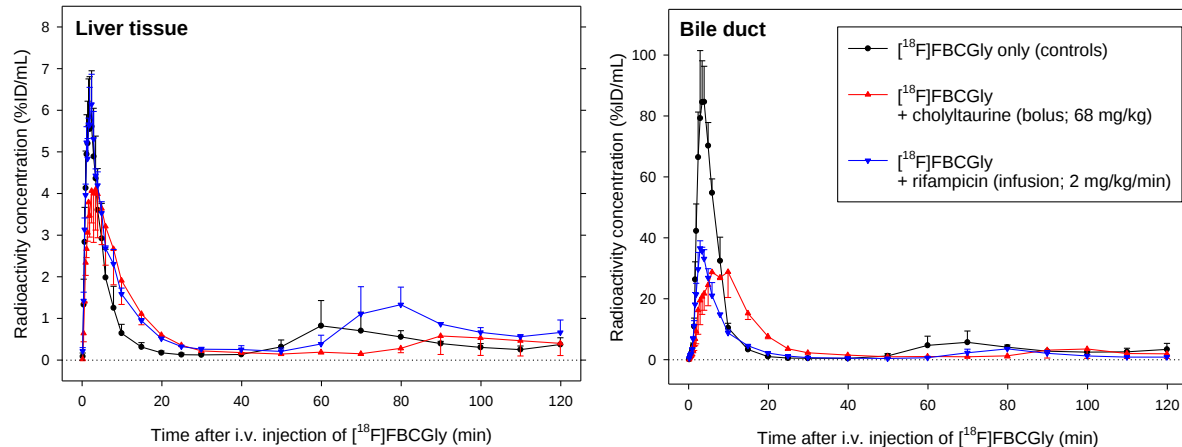
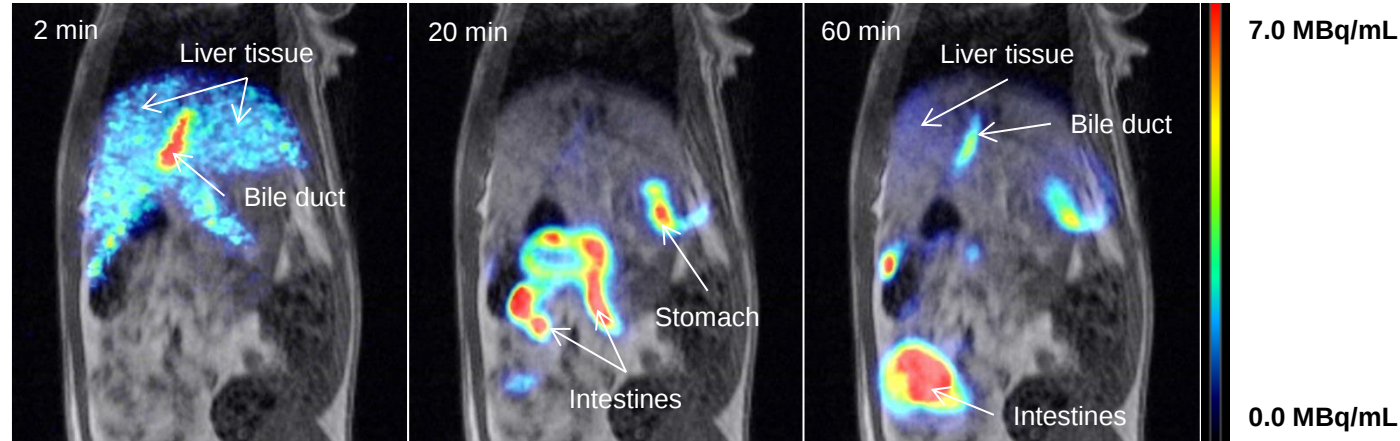
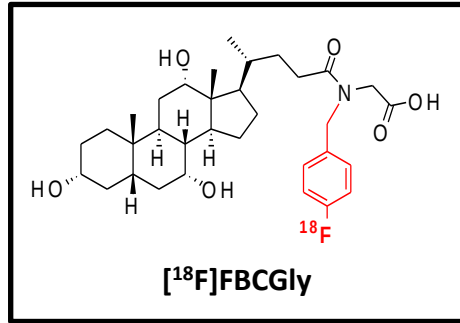
Enterohepatic circulation of [^{18}F]FBCGly in rats

Dynamic PET/MR recorded after i.v. injection of [^{18}F]FBCGly in Sprague-Dawley rats



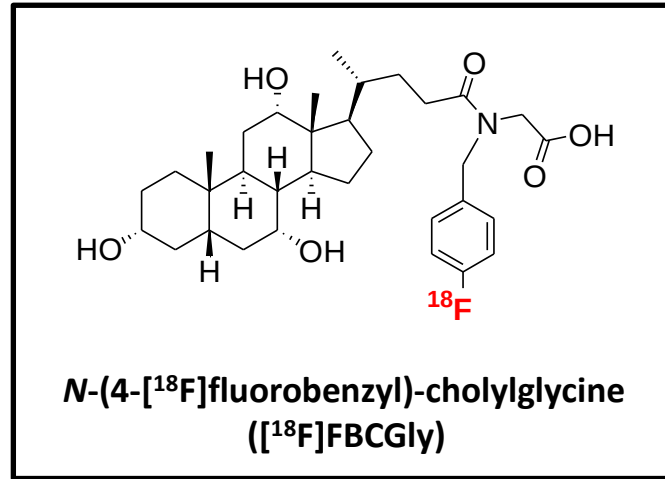
Enterohepatic circulation of [^{18}F]FBCGly in rats

Dynamic PET/MR recorded after i.v. injection of [^{18}F]FBCGly in Sprague-Dawley rats



Conclusion

- [^{18}F]FBCGly is a novel ^{18}F -labelled bile acid PET-tracer derived from cholylglycine
- Similar to [^{11}C]cholylsarcosine, [^{18}F]FBCGly is rapidly taken up by the liver and excreted into bile
- [^{18}F]FBCGly undergoes enterohepatic circulation without metabolizing



Outlook:

- [^{18}F]FBCGly as tracer for PET of patients with cholestatic liver diseases and bile acid malabsorption
- [^{18}F]FBCGly PET as tool in drug development (*e.g. in vivo transporter studies*)