efpia

European Federation of Pharmaceutical
Industries and Associations

Improve the Impact of Imaging Solutions on Drug Safety Evaluation

Gunnar Schütz, Bayer Healthcare, Berlin
SGG Translational Safety

Non-Cinical Development – Problem Statement

* 43% concordance between clinical trial toxicities & rodent toxicity seen across 150 compounds; 63% in non-rodents

* Clinical toxicity predictions vary by organ system as well as species dropping to as low as 36%

Ohlsen et al., Reg Toxicol Pharmacol 2000, 32: 56-67

* How can we guard against drug-induced injuries in the clinic *but not in preclinical toxicological studies?*

* How can we advance development of good drugs showing toxicities in animals *that are not expected to be present in humans?*

* How can we verify efficacy in preclinical *and* clinical settings?

Challenge: Systematic translation of new imaging methods

Imaging "can":

* DCE-MRI
* X-nucleus MRI
* Diffusion MRI
* MR-Spectroscopy
* Dual-Energy CT
* Perfusions CT
* ….

Currently used parameter in the Clinic:

**Translation?
Evidence?
Validation?**

* RECIST

* Gap between available technology and clinical routine
* *Vision*: Implement imaging biomarkers as integral part of clinical trials and clinical routine

efpia

MR Imaging of Brain Structure and Function

✳ Detection of changes in **anatomy** at high resolution (tissue size)

✳ Functional information on tissues (perfusion, oxygenation, diffusion, **spectroscopy**)

✳ Possibility to perform **longitudinal** studies (reduces animal number)

Rodent brain tissue
MRI compared to
histology

Calabrese et al. Neuroimage 2013, 67:375-384

Rodent brain spectroscopy in a
huntington's disease model

Journal of Neurochemistry 2006, 100 (5):1397-1406

efpia

MR Imaging of Kidney Function

* Detection of changes in contrast agent **excretion kinetics**
* Functional information: **oxygenation**
* **Longitudinal** study (reduces animal number)

CT of rodent kidney
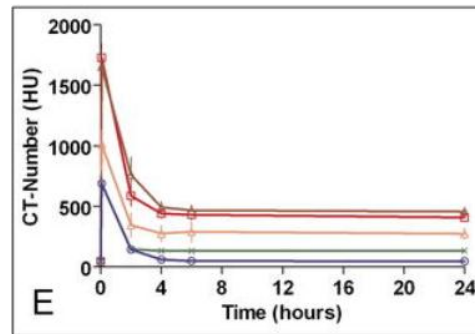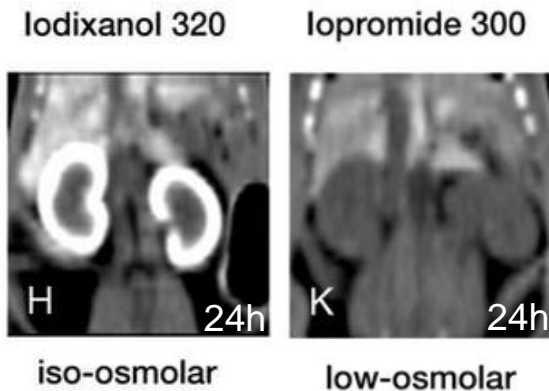
Blood oxygenation level dependent (BOLD) MRI of rodent kidney
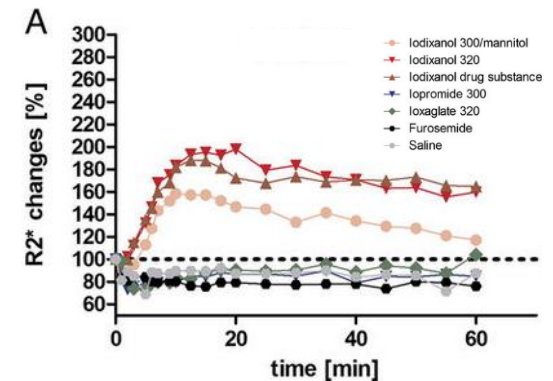
Lenhard et al., Invest. Radiol. 2013, 48(4):175–182

* BOLD-MRI is considered one of the earliest biomarkers for kidney injury

Validation of Diagnostic Imaging Techniques for Their Use in Clinical Drug Development

* We need technically, biologically and clinically validated imaging biomarker techniques

* What is needed for validation?

    * Technical standardization of imaging method & procedure
    * Technical standardization of image evaluation and read-out
    * Pre-clinical validation against currently accepted measures
    * Prove robustness and informative value in animal disease models
    * Translation to patients; confirm robustness and informative value

* Need for public private partnership to establish and extend the basis for imaging biomarker utilization in patients

efpia

Value of Clinically Validated Imaging Biomarker

* For patients:
    * Improved basis for therapy decision
* For pharmaceutical industry:
    * Perform longitudinal studies: reduce number of animals used
    * Identify potential safety/efficacy issues earlier: enable earlier project decision (avoid respective late phase investments)
* For imaging equipment vendors
    * Intensified use of imaging in pharmaceutical development
    * Enable use of imaging biomarker as integral part of clinical routine
* For software providers
    * Novel qualified tools for data analysis and reporting
    * Image data analysis across patients for procedure refinement

efpia