Medical Imaging in Early Phase Trials

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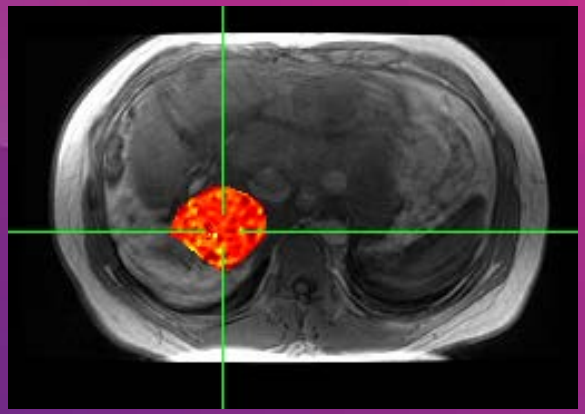
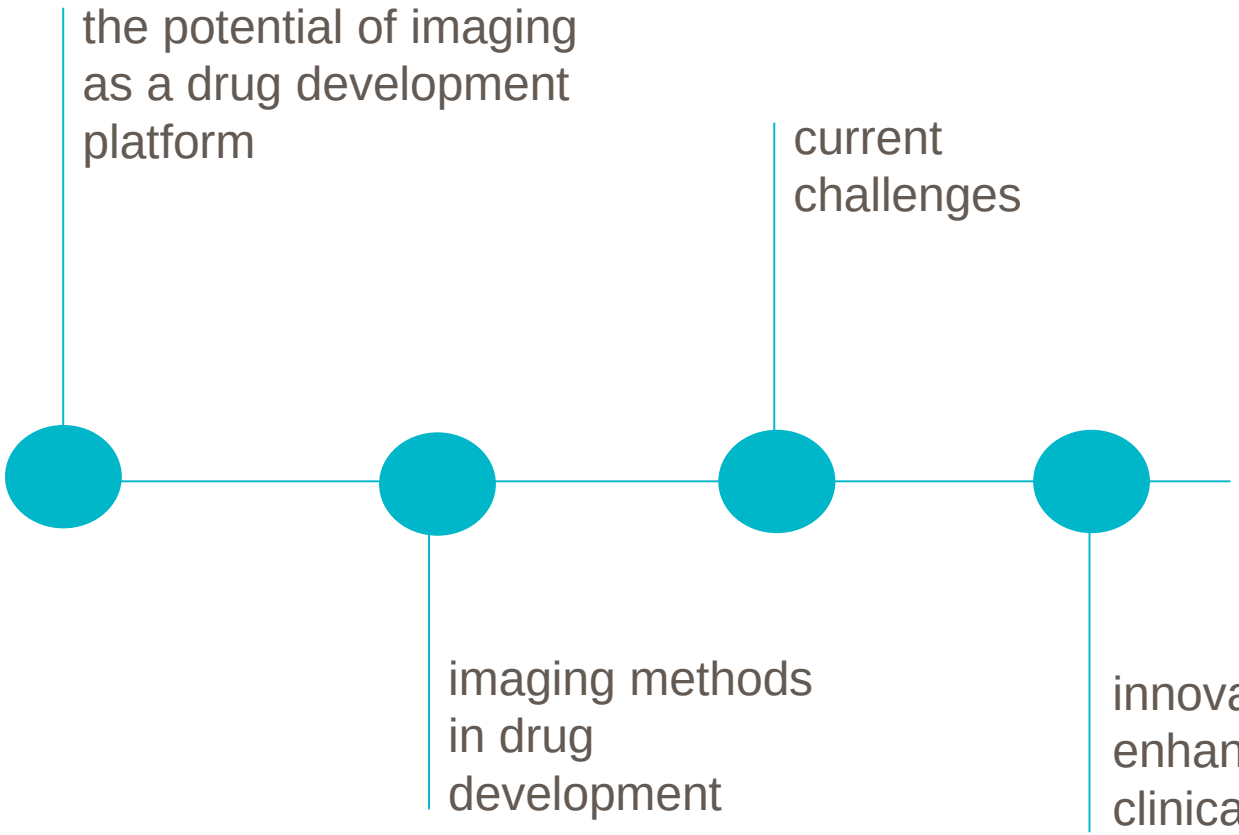


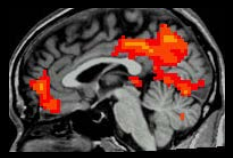
Imaging Innovation for Early Phase Trials



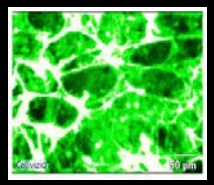
The potential: whole-body molecular, functional and structural imaging for drug development

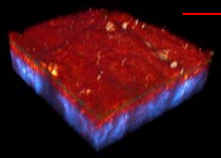
whole-body disease characterisation

functional brain imaging to study symptoms

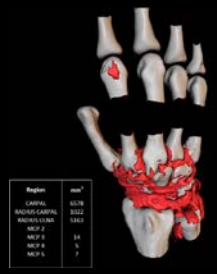


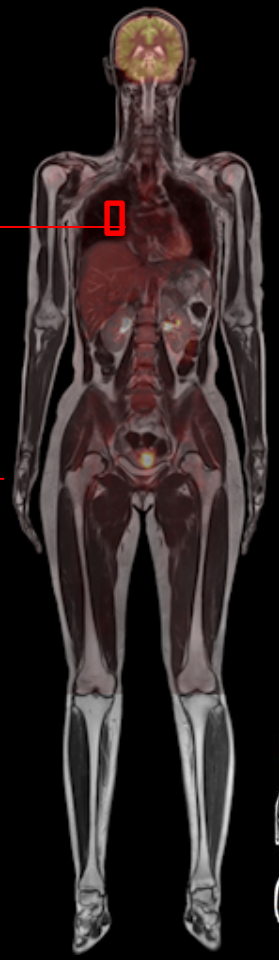
in vivo microscopy + / - probes

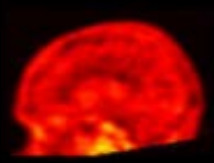




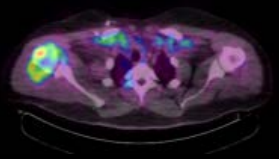
in-stream quantification to extract endpoints





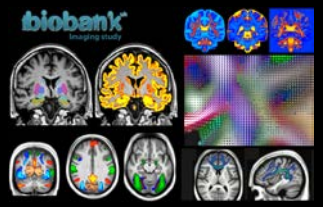


small molecule and antibody bio-distribution

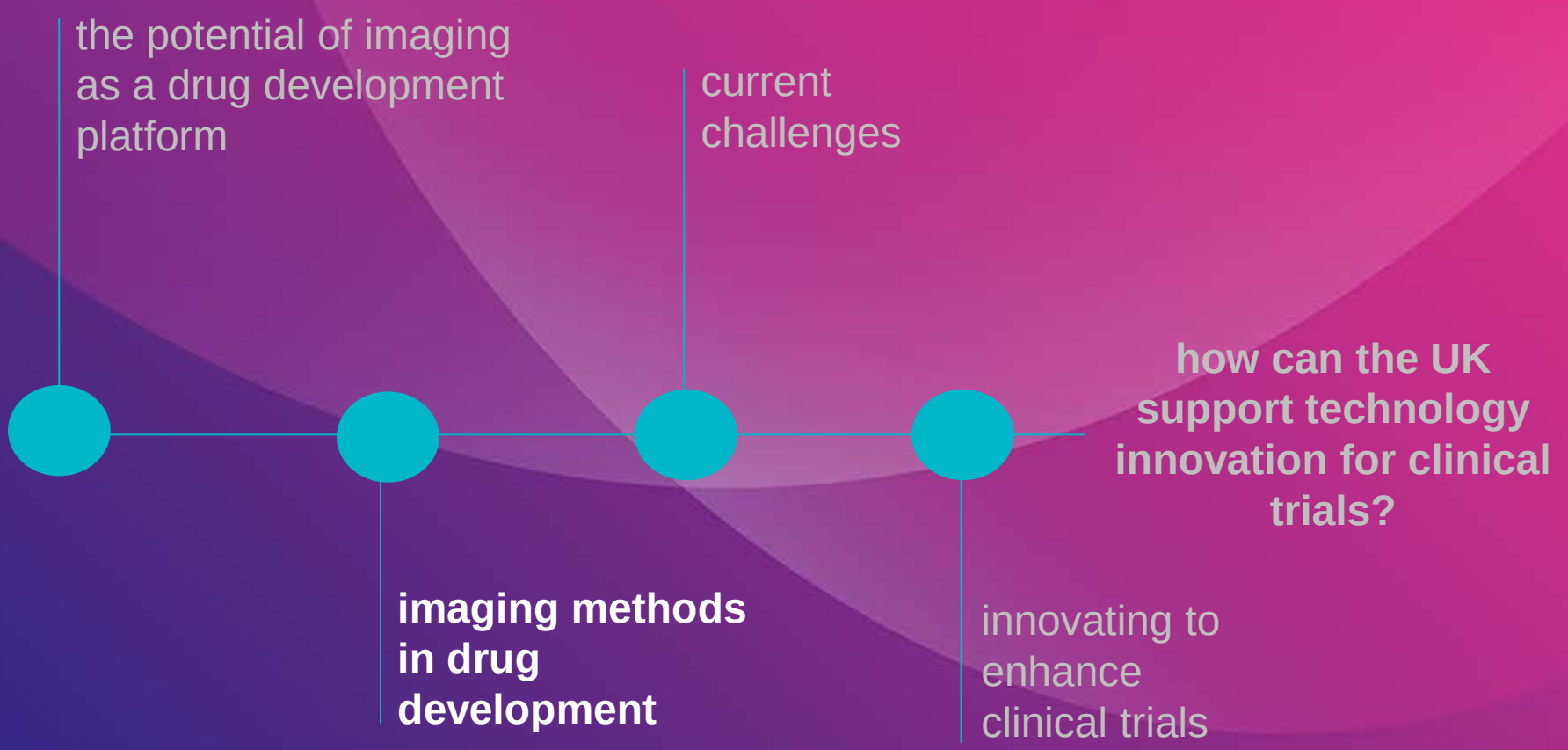


target engagement- beyond neuro

a range of molecular and cellular probes



analytics linking to normative databases supported by AI


the potential of imaging as a drug development platform
current challenges
how can the UK support technology innovation for clinical trials?
imaging methods in drug development
innovating to enhance clinical trials

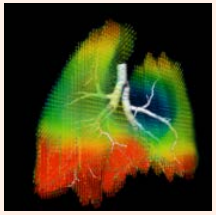
Contrasting demands on imaging technology

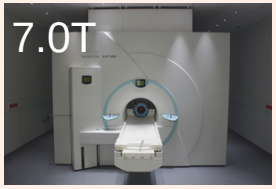
Early versus late phase drug development

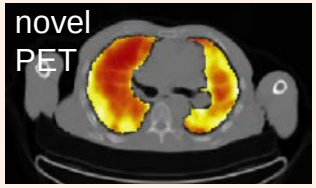
Specialisation- cutting edge
Single centre, e.g. N=4

Simplification- enable access
Tens to hundreds of centres

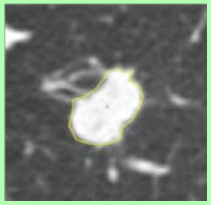
Experimental Medicine

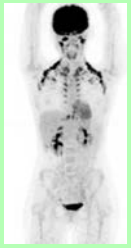


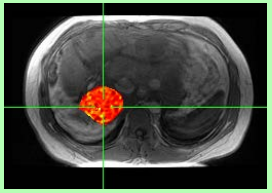




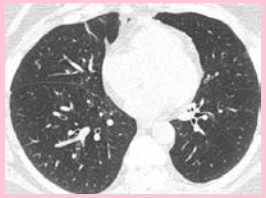
Phase II

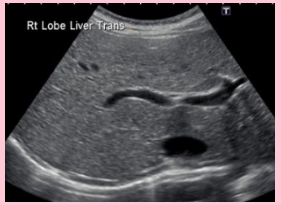


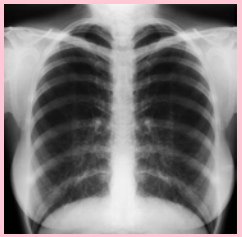




Phase III, screening, diagnostics

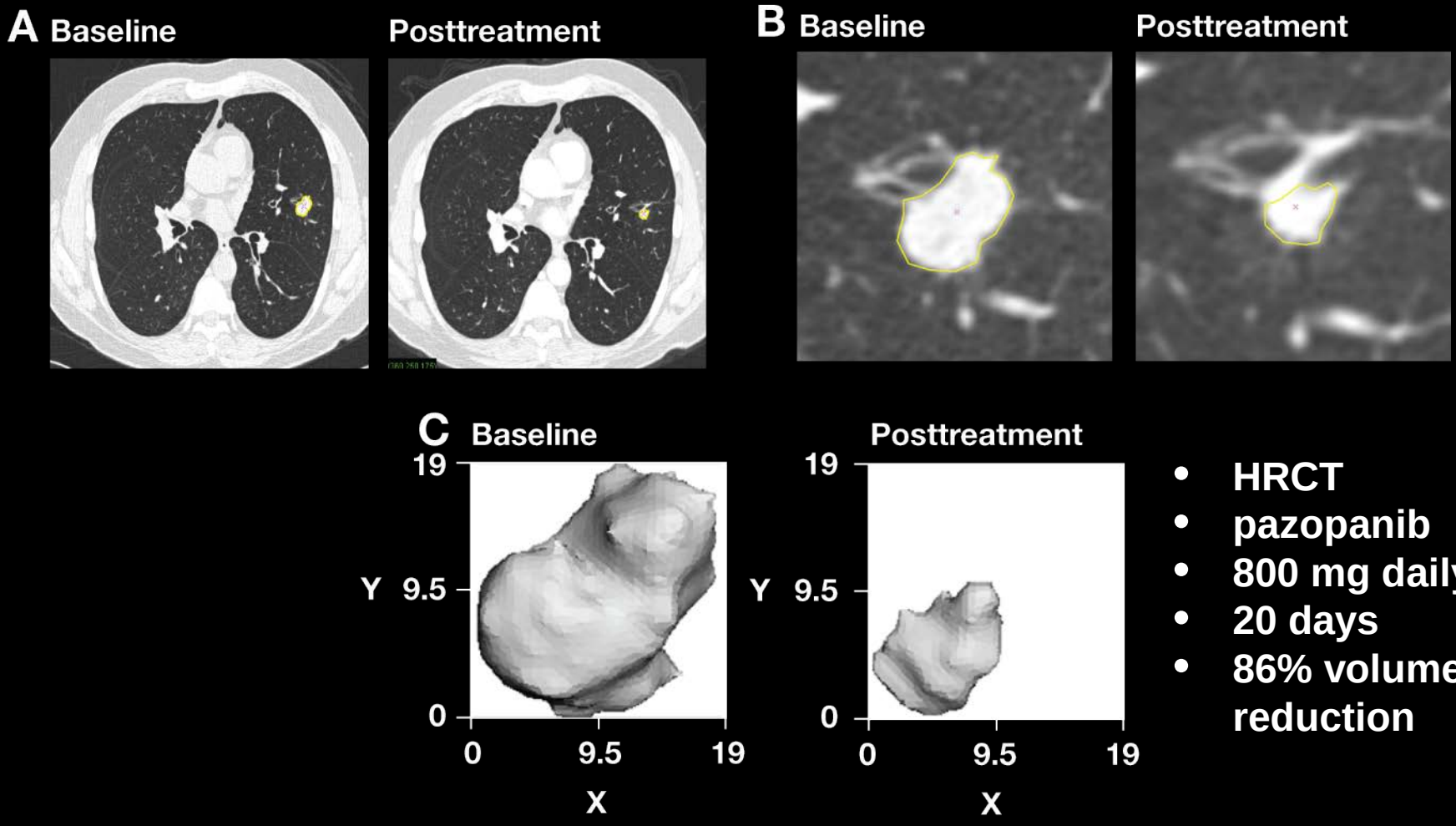






Imaging structural change

Oncology disease response assessment

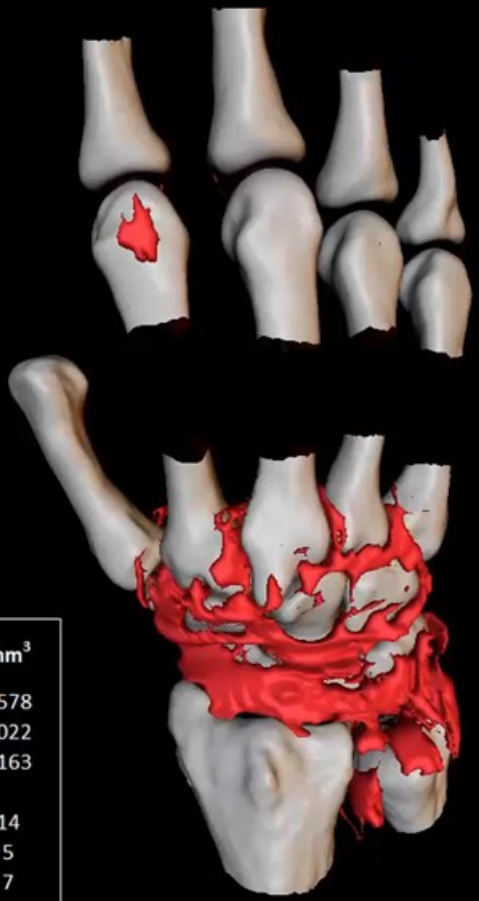


- HRCT
- pazopanib
- 800 mg daily
- 20 days
- 86% volumetric reduction

Altorki et al., Journal of Clinical Oncology, 2010, **Phase II Proof-of-Concept Study of Pazopanib Monotherapy in Treatment-Naïve Patients With Stage I/II Resectable Non–Small-Cell Lung Cancer**

Downstream markers of pharmacology

Studying inflammation with high quality MRI and quantitative analysis



Region	mm^3
CARPAL	6578
RADIUS CARPAL	1022
RADIUS ULNA	5163
MCP 2	
MCP 3	14
MCP 4	5
MCP 5	7

Rheumatoid arthritis MRI score: RAMRIS

RAMRIQ: quantitative scoring method to improve performance
Bowes et al., ACR/ARHP, 1178, 2014

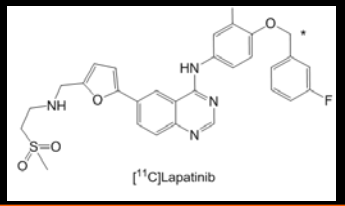
Includes quantification of synovitis volume based on gadolinium contrast enhancement

imorphics

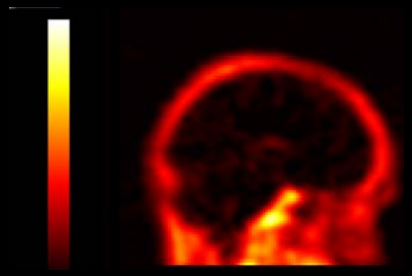
courtesy of Dr. Mike Bowes

Studying drug exposure

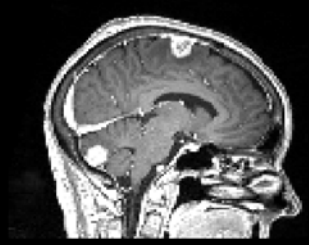
Radiolabelled drug and Positron Emission Tomography

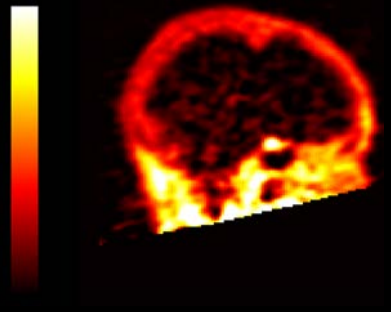


Normal brain

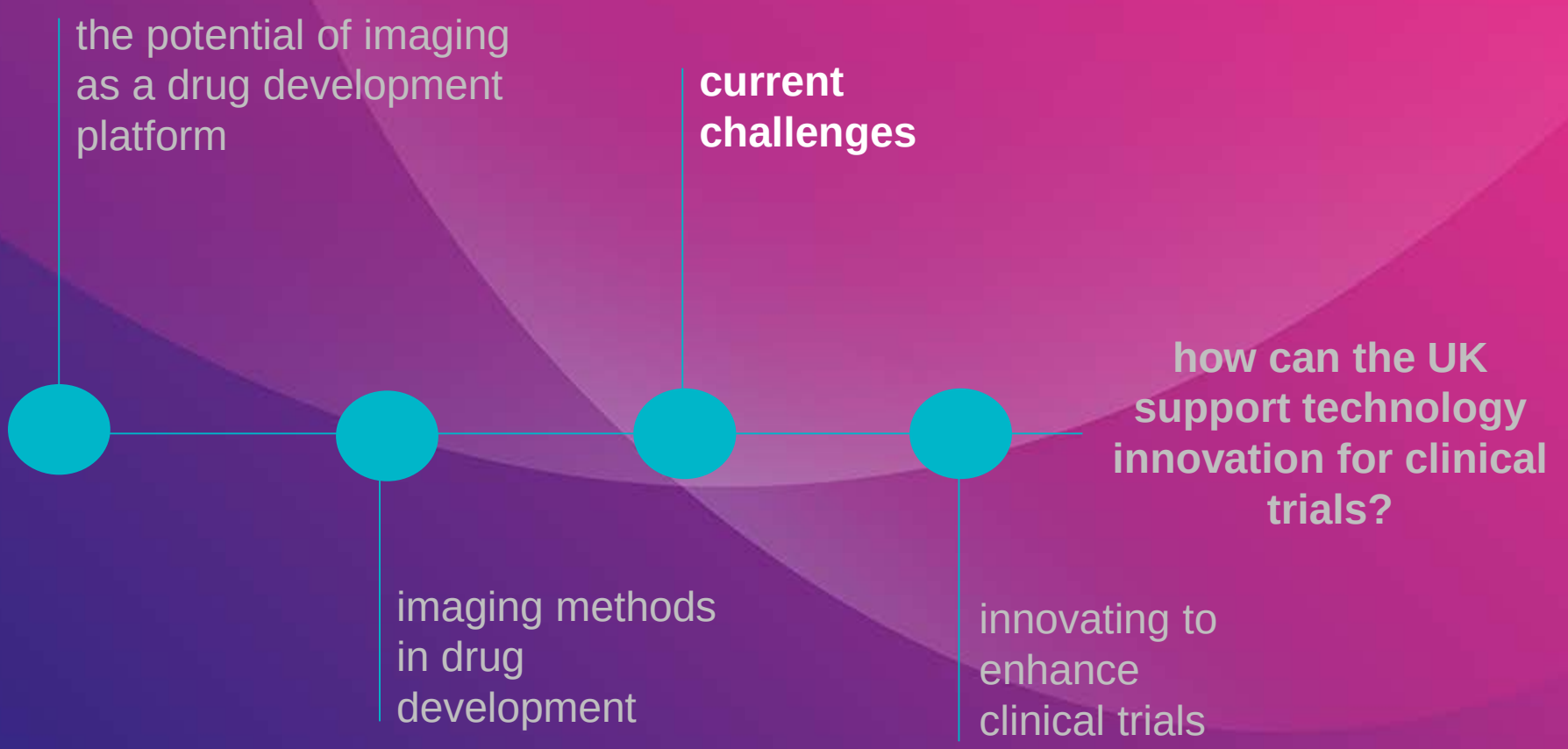


Metastases





[11C]-lapatinib access into normal brain and brain metastases in patients (n=6) with Her-2 over-expressing breast cancer, EJNMMI Res., 2015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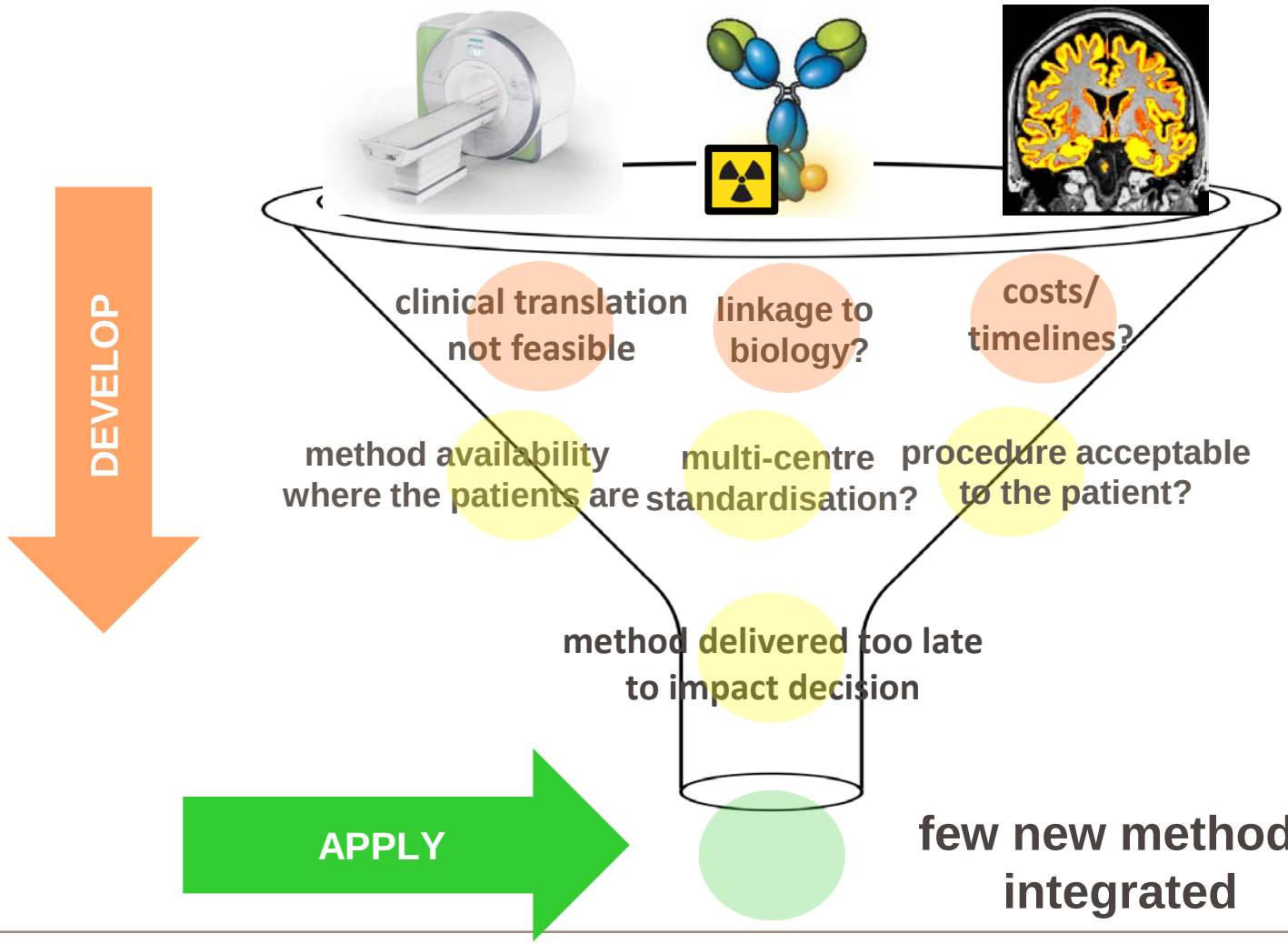
What is limiting broader use of clinical imaging tools?

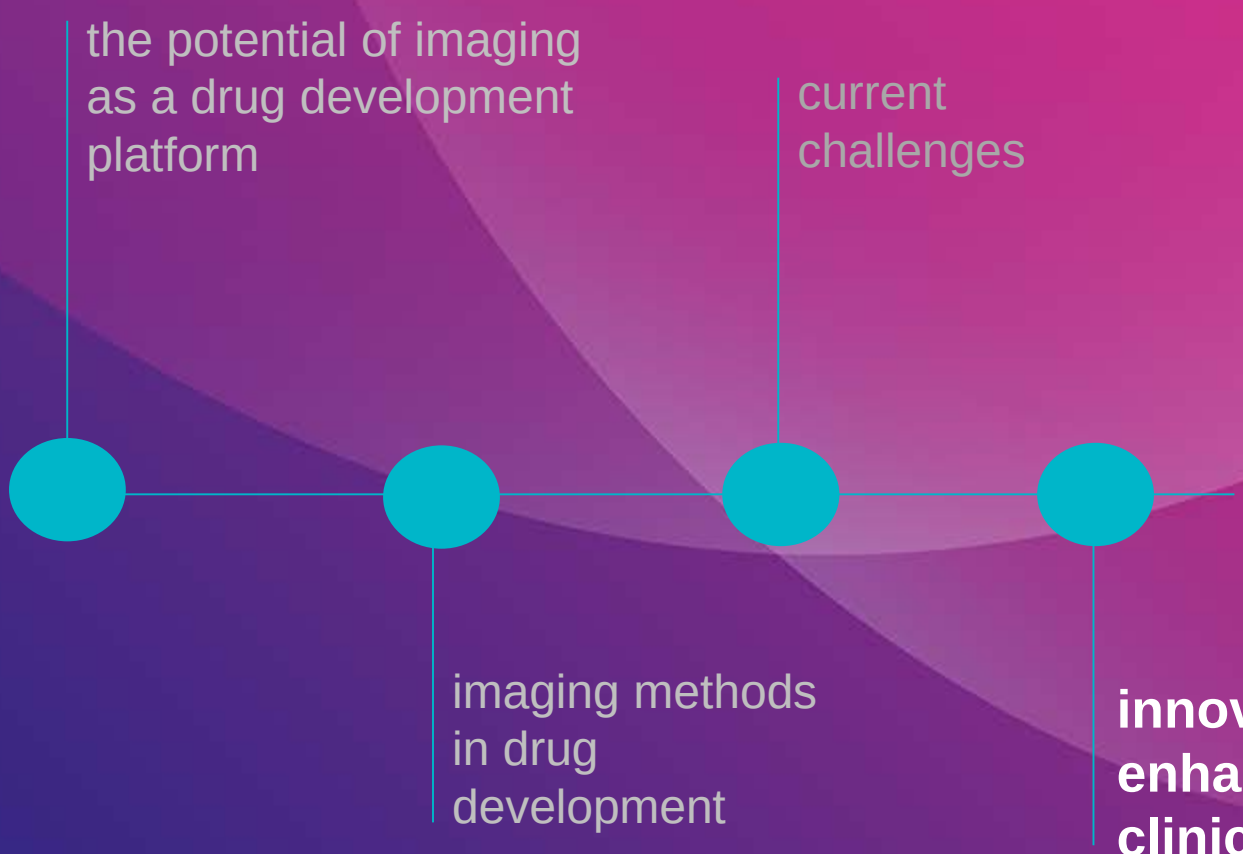
- More awareness of potential, increased demand
- Many potential methods: probes, hardware, analysis
- Academia engaged in developing new methods

- Too few measures of pathophysiology / mechanism
- Moving methods into the clinical is slow/costly
- Insufficient confidence in some methods for decision-making

Only a small proportion of potential methods become drug development tools



Has molecular imaging delivered to drug development?
Murphy et al., Phil.Trans.A, 2017.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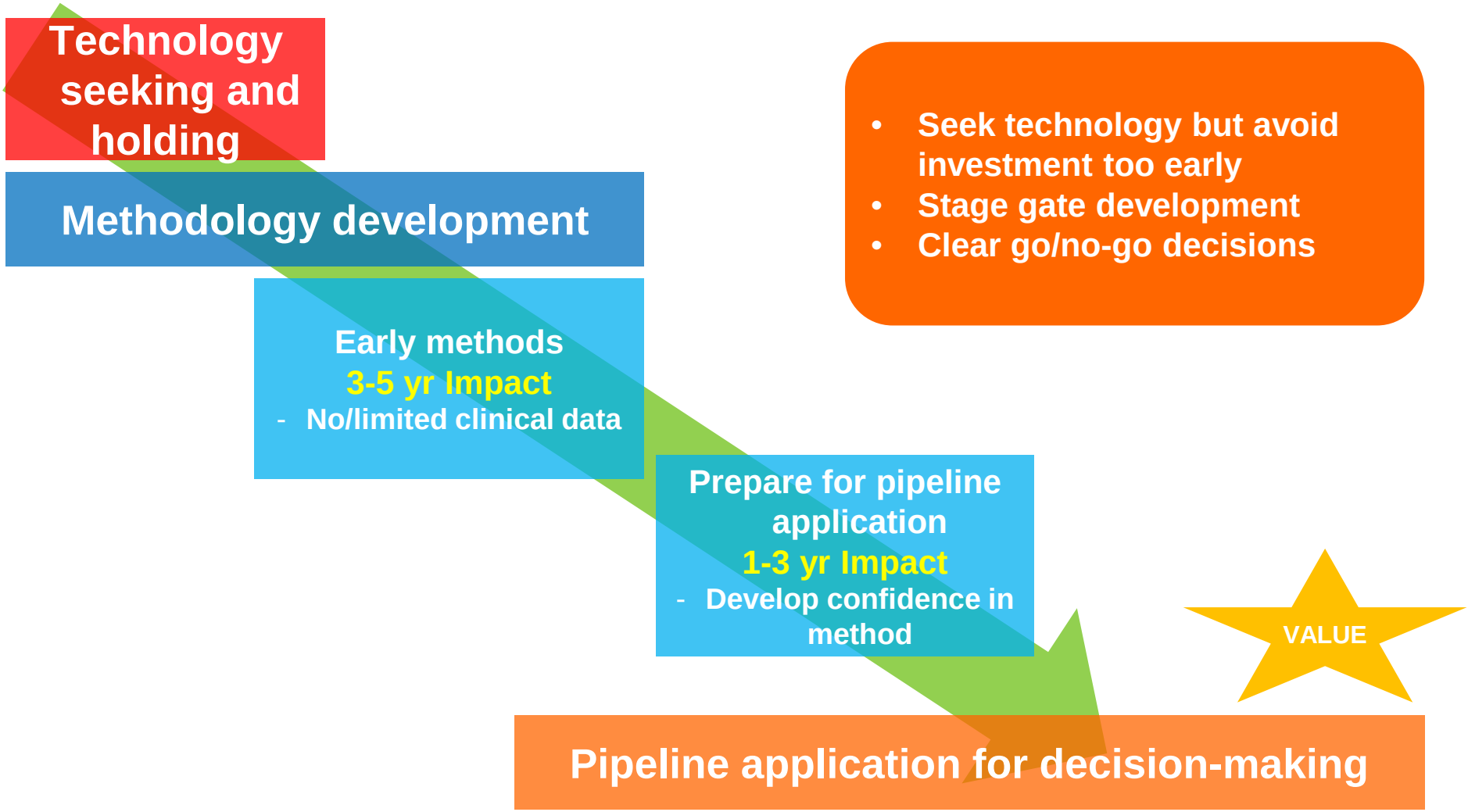
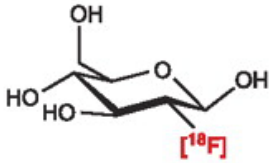
Mapping technology development towards clinical impact

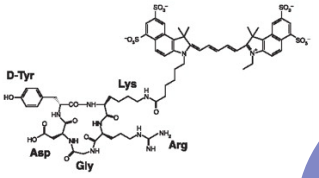


Probe chemistry and the molecular imaging experiment

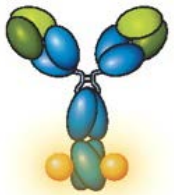
small molecule



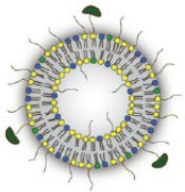
peptide



antibody

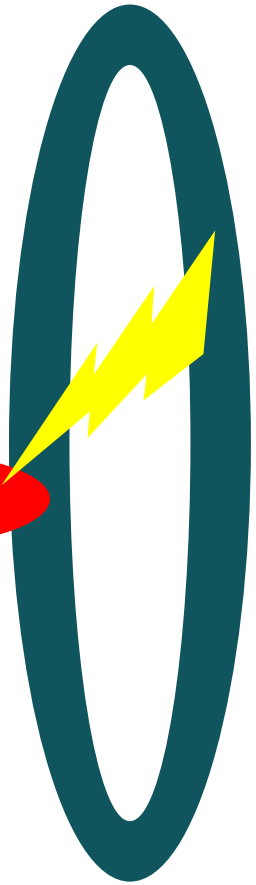


nanoparticle



bio-molecule or particle

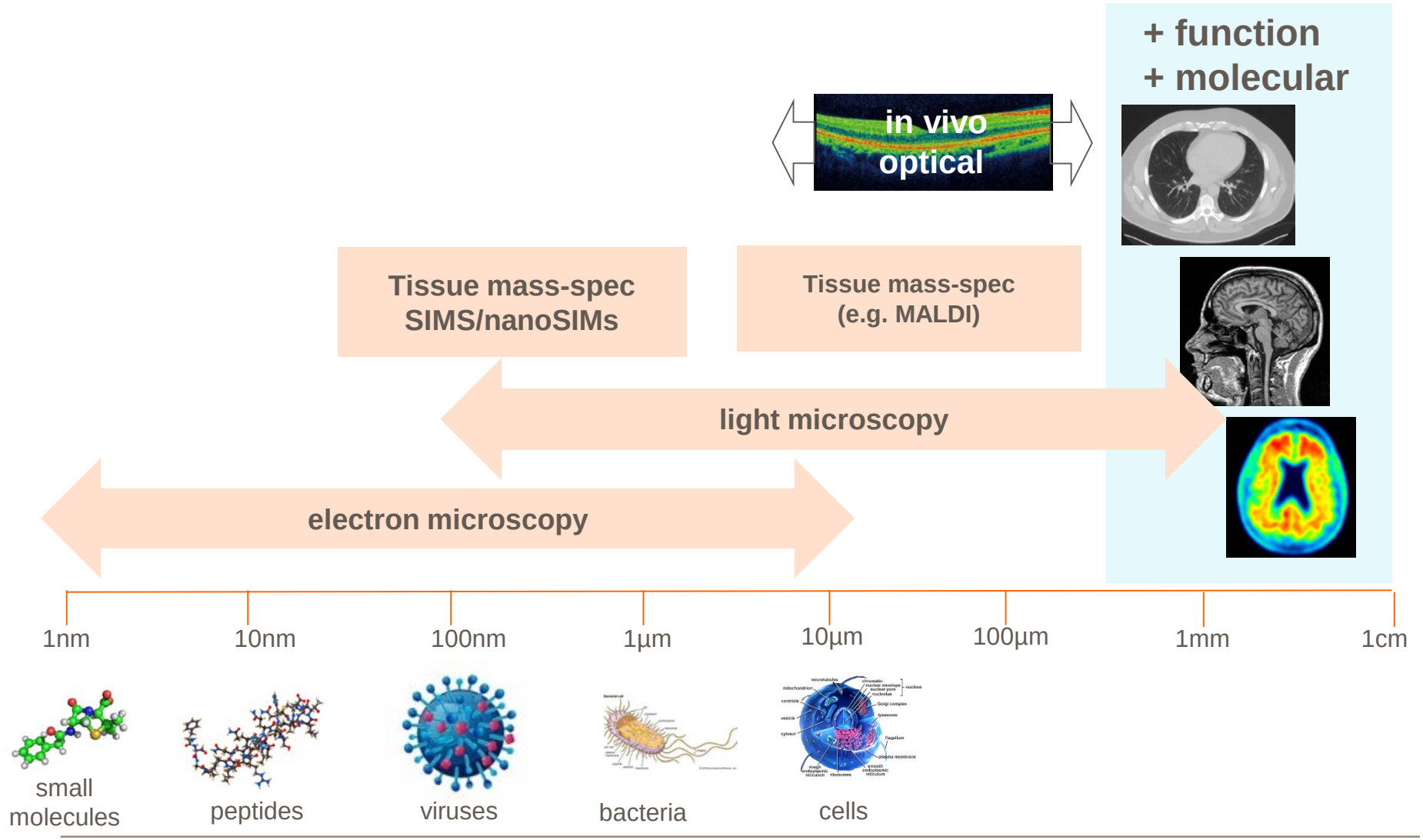
signal



detection

Can we further understand our in vivo measurements?

Imaging across different scales



Technology to Support Early Clinical Development

How can we optimise the interface?

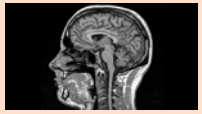
Pharma R&D
Therapeutic areas: indications, mechanisms, therapeutic platforms

Interpret many, changing needs

View now, 1-3yrs, +5yrs

Internal technology interfaces

Biomarkers



Data analytics

Devices

Imaging

Distributed expertise

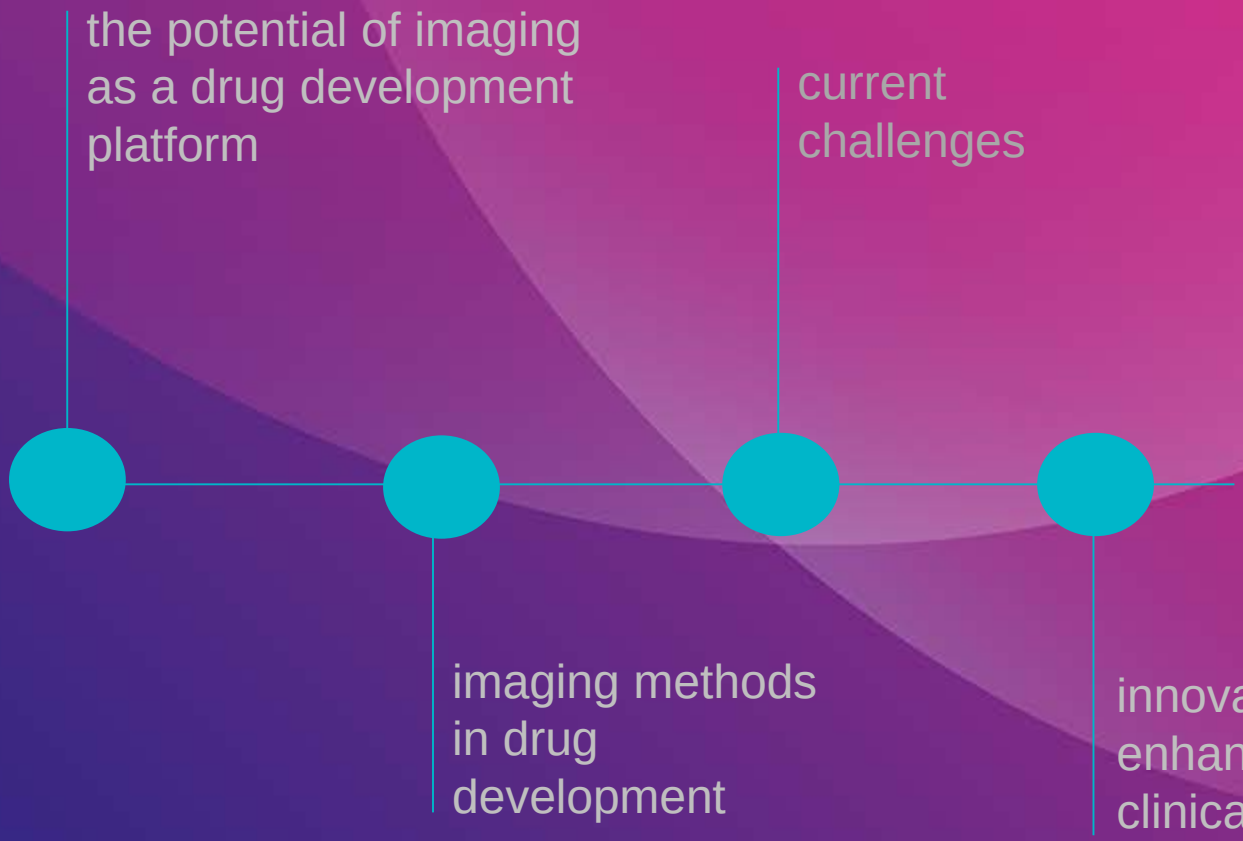
External technology landscape

Academia

Commercial Diagnostics

CROs

Complex, changing external network



how can the UK support technology innovation for clinical trials?

Translation of imaging technologies to drug development in the UK

Magnetic Resonance:
- Many leading clinical MRI centres
- High-field (7T) MRI network
- Dementia Platform UK – PET/MR network
- Expertise in hyperpolarised methods

Molecular imaging:
- Commercial and academic
- Novel clinical radiochemistry
- Leading PET centres
- Chemistry

Optical imaging:
- Clinical optical expertise
- Rosalind Franklin Institute –new technologies

Imaging science training:
- EPSRC Centres for Doctoral Training

Data sciences:
- Alan Turing Institute
- UK Biobank

Optimising technology for clinical drug development

- **Networks to ensure technology is available in clinical centres**
  - shipping radiotracers or transfer methods for local production
  - standardised scanning protocols and analysis/reporting
- **Imaging technologies must be pulled from silos**
  - multi-modality and across scales
  - access basic sciences to solve problems – e.g. chemistry for probes
- **Data as a central theme**
  - enable sharing, meta-analyses, automated analyses
- **Consider complex versus scalable measurement technologies**
  - blood biomarkers developed using imaging
- **Connect technology expertise to drug development**
  - train a new generation of imaging scientists
  - drug development community must challenge technologists
- **Ensure imaging has a clear path towards decision-making**