Queen's University Belfast

CCRCB
Centre for
Cancer Research
& Cell Biology

Overview of Research from the Centre for Cancer Research & Cell Biology, Queen's University Belfast

Kevin M. Prise

Centre for Cancer Research and Cell Biology (CCRCB)

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www.qub.ac.uk/ccrcb

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Northern Ireland
Clinical Cancer Centre

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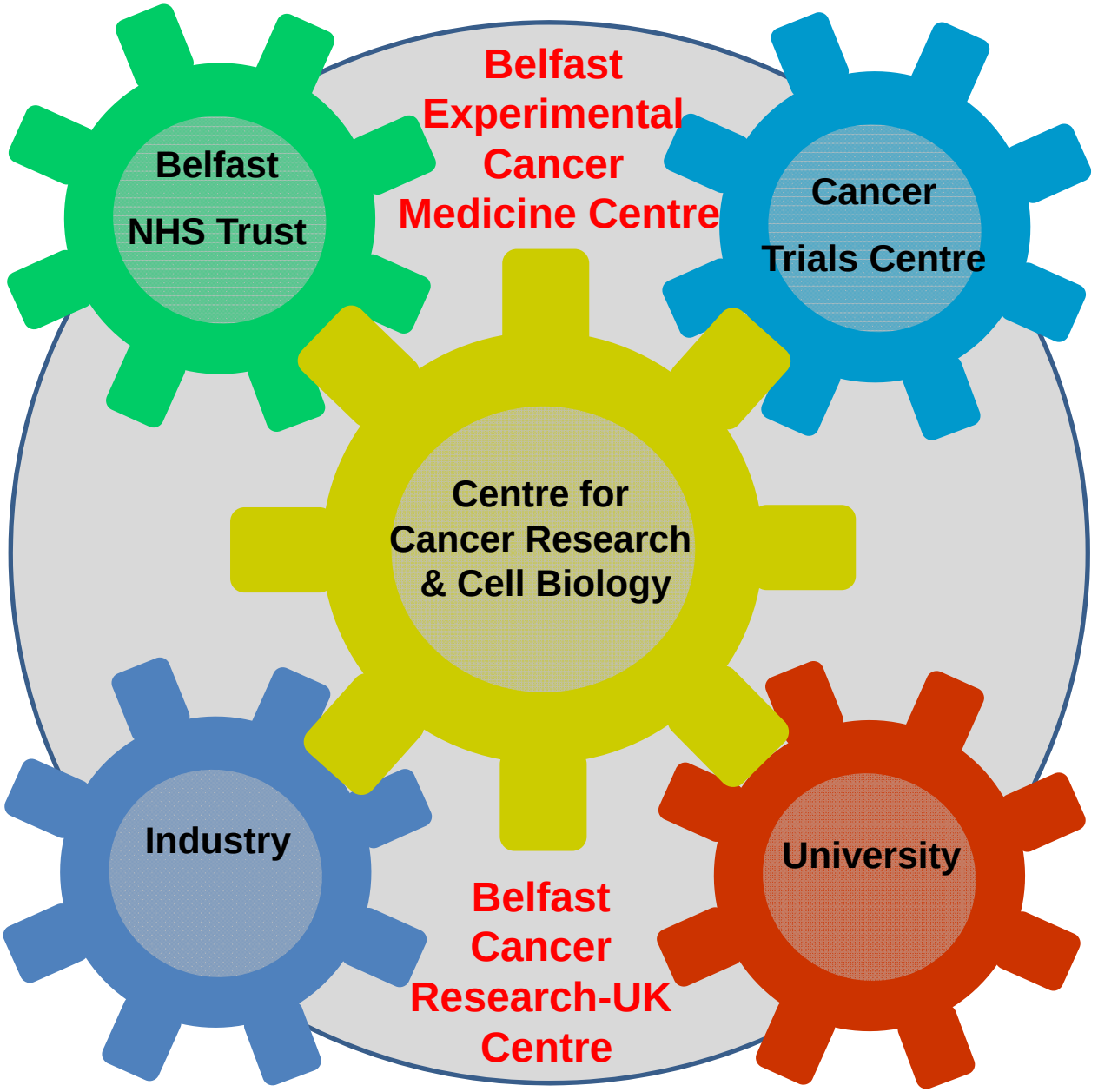
Cancer Research at CCRCB



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Mission Statement

CCRCB
Centre for
Cancer Research
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Our mission is to improve patient care through the development of:

- Biomarkers – for prognosis, prediction and markers of response
- Biologically determined targeted therapies

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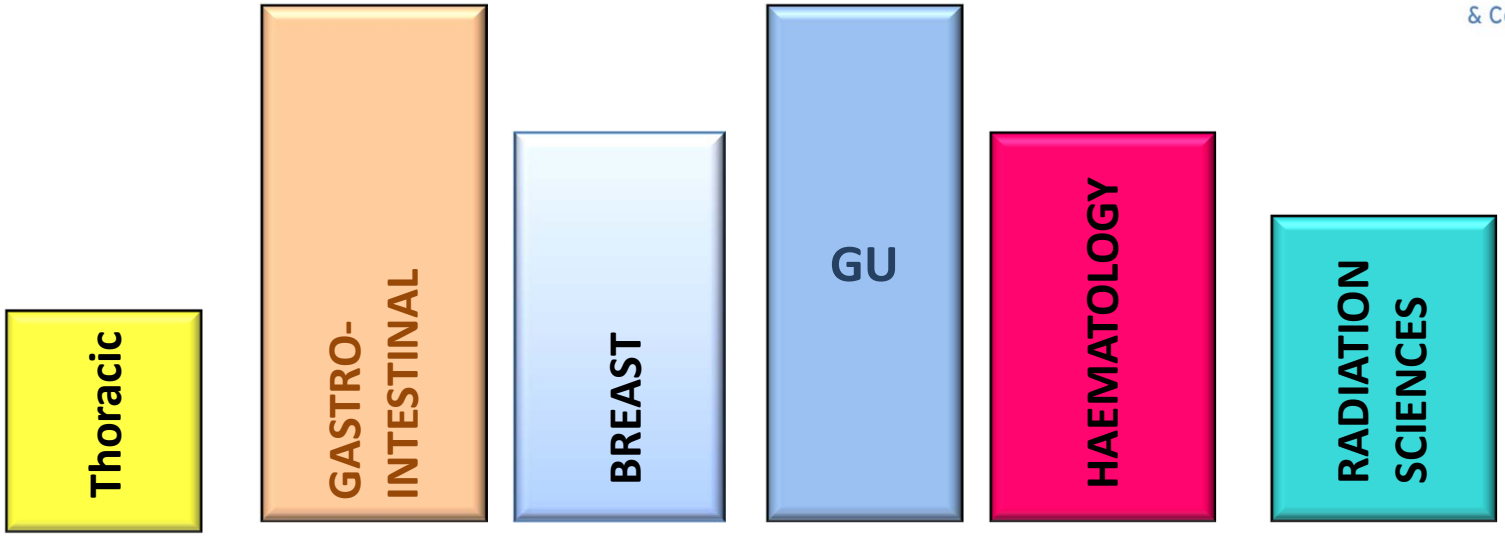
Focus Groups



Enabling Technologies

BIOINFORMATICS and IMAGING

PATHOLOGY/TUMOUR BANK

DRUG DISCOVERY

CLINICAL TRIALS

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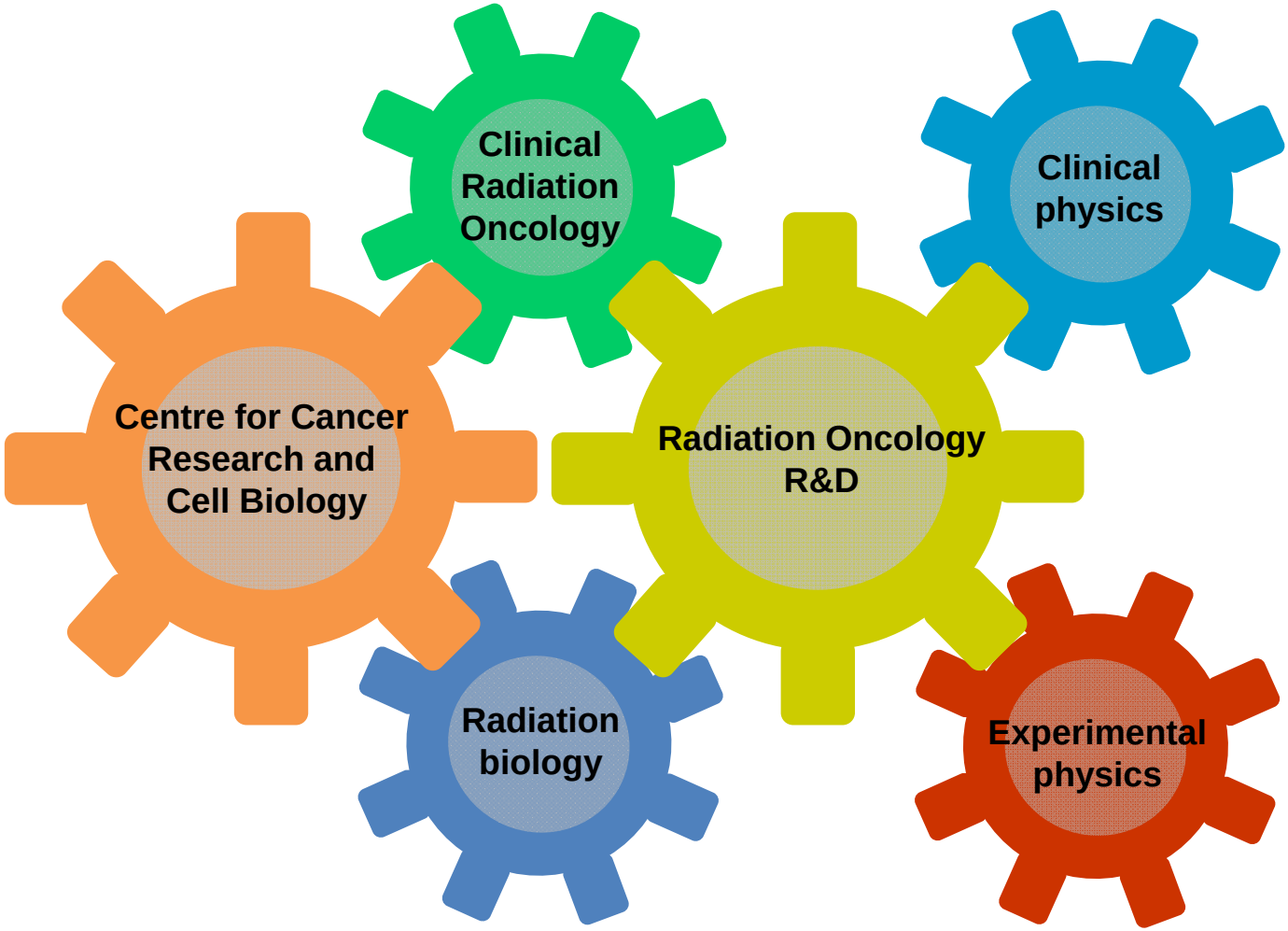
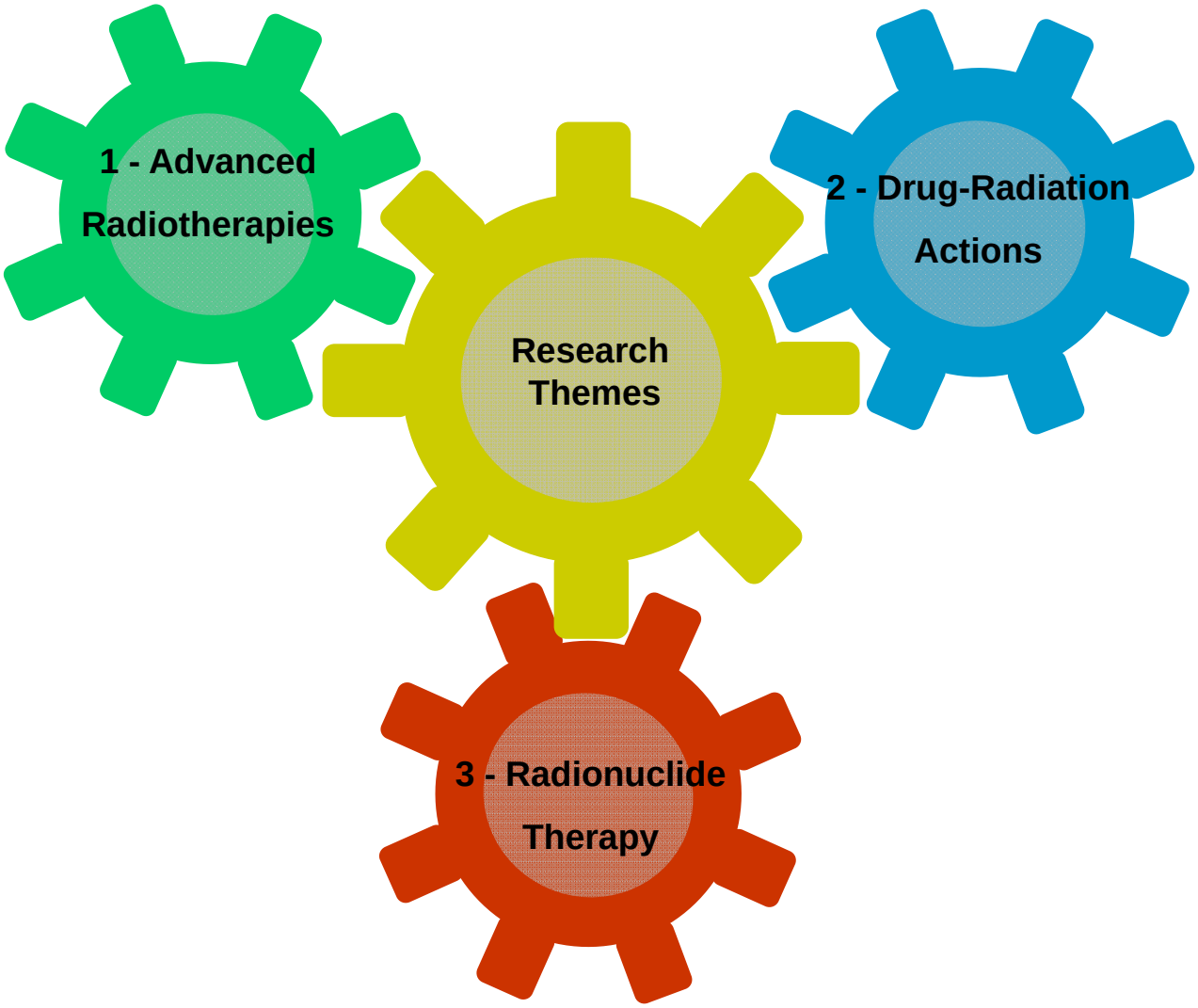
Radiation Science at CCRCB



School of Medicine, Dentistry and Biomedical Sciences
School of Mathematics and Physics
School of Pharmacy
School of Biological Sciences
School of Chemistry

Northern Ireland Cancer Centre
Depts of Radiation Oncology and Radiotherapy Physics
Northern Ireland Cancer Trials Centre

Radiation Sciences - Research Themes



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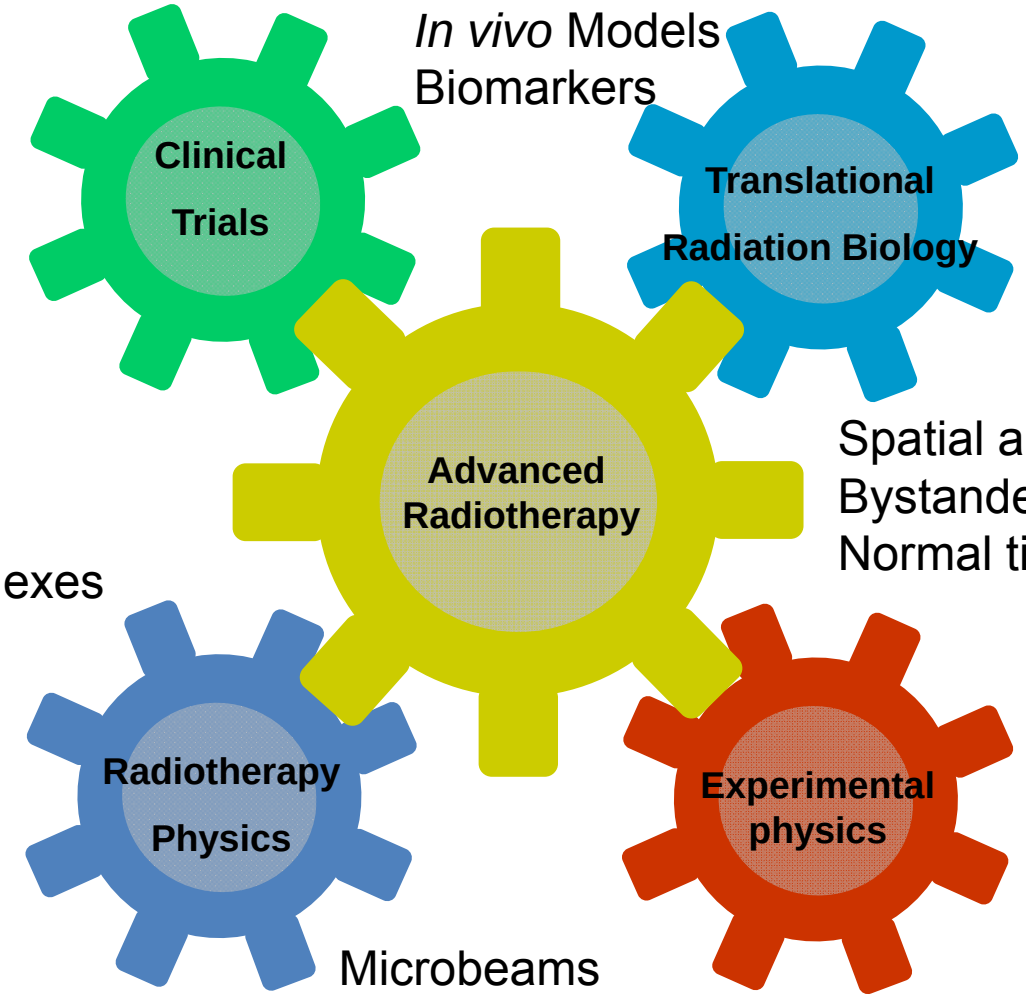
Theme 1 – Advanced Radiotherapy



In vivo Models
Biomarkers

CHiPP trial
IMPORT
Stereotactic
Complexity indexes
Data mining

Spatial and temporal effects
Bystander signalling
Normal tissue responses

Microbeams
Charged Particles
Anti-protons
Monochromatic photons

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Clinical Research in Radiation - Belfast

External Beam - Prostate

- PRO7
- CHHiP
- Prostate Bladder scan study 1+2
- MRI – CT Fusion study
- Radiation Biomarker study
- EORTC 22991
- Prostate cancer RT QoL study
- Radicals
- STAMPEDE

Bone seeking Radionuclide

- Taxium 1 + 2
- Alpharadin phase 2 + 3

External Beam - other sites

- Spinal Cord Compression study (all cancer)
- Cabernet Study (Macular Degeneration)
- BC2001 (Bladder)
- PETCT (Lung)
- QUARTZ (Lung)
- IMPORT LOW (Breast)
- ACT II (Anal)
- PRIME (Uterus)
- SUPREMO (Breast)
- ART DECO (H&N)
- ARISTOTLE (Rectal)

Clinical lead: Joe O'Sullivan

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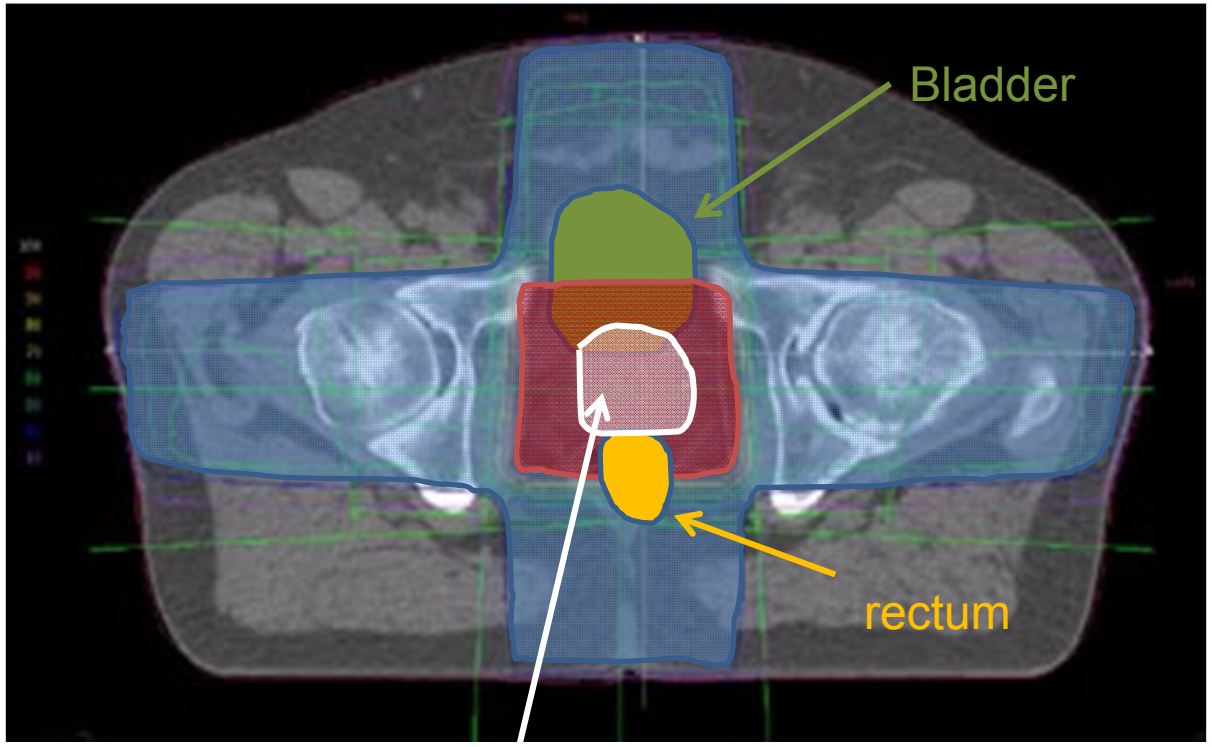
Conventional Radiotherapy

- A few beams are directed to the target to give a uniform dose over a large area (which includes the tumour)
- A large volume is exposed to high radiation dose

Conventional External Beam – 3D-Conformal Radiotherapy (3D-CRT)



Low dose volume

High dose volume

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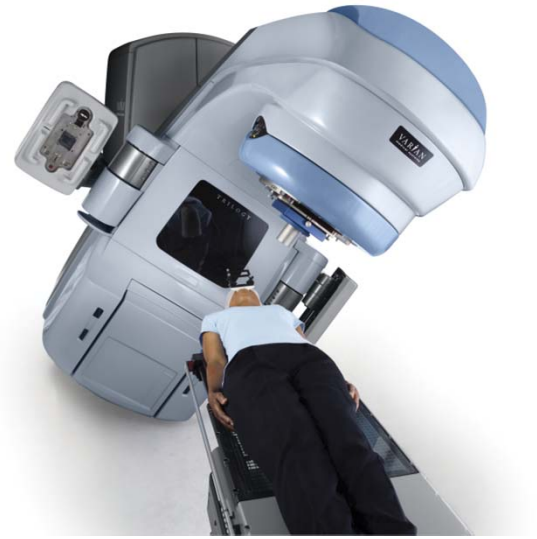
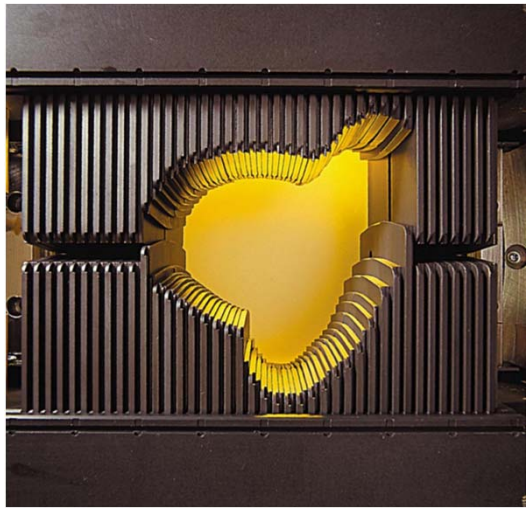
Clinical linacs for radiotherapy

- For radiotherapy mostly high energy X-rays (6 – 20MV) are used generated from a linac
- The treatment head rotates around the patient
- In the head of the linac a multileaf collimator consisting of interleaved tungsten leaves can be used to shape the beam





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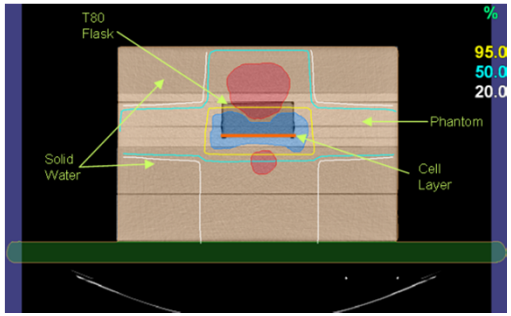
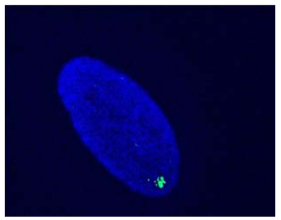
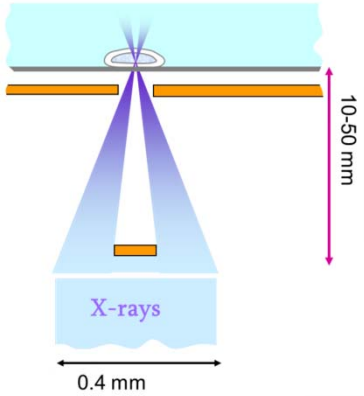
New biological models for advanced radiotherapy

- Test biological effectiveness of clinically relevant spatial and temporal radiation exposures
- Determine the impact of bystander signalling and underlying mechanisms
- Develop new *in vivo* models for testing clinically relevant protocols
- Develop new metrics for treatment planning of advanced radiotherapy from TCP/NTCP







Kevin Prise / Stephen McMahon / Giuseppe Schettino / Joe O'Sullivan / Alan Hounsell

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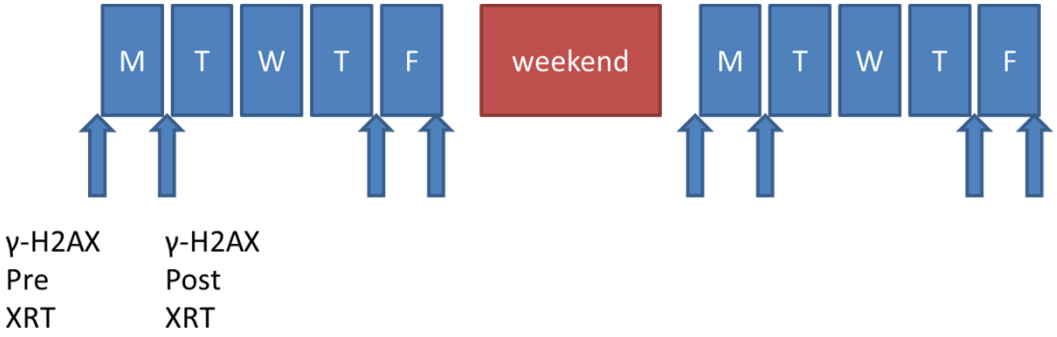
Biomarker / Biodosimetry Studies

- For advanced radiotherapies suitable biomarkers need to be developed which can be used as surrogates for treatment efficacy

Aims

- Undertake a clinical study is assessing a DNA damage markers as biodosimeter and biomarker in patients undergoing prostate radiotherapy and brachytherapy
- Develop studies with markers of normal tissue damage



Darren Brady, Kevin Prise, Joe O'Sullivan

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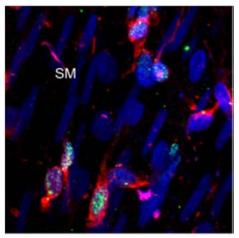
Bladder Toxicity

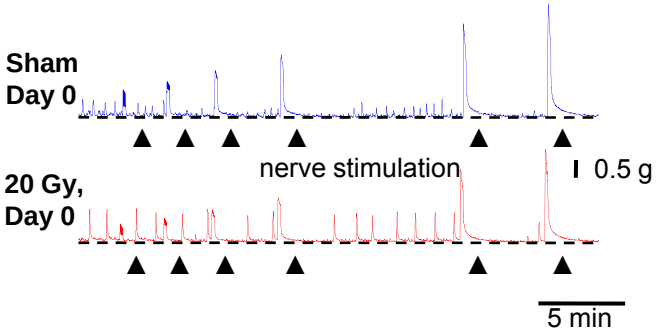
- For advanced radiotherapy of the prostate the bladder is a limiting normal tissue
- Mechanisms of toxicity are poorly understood

Aims:

- To investigate the cellular and molecular basis of radiation induced bladder dysfunction using targeted irradiation approaches
- To investigate the potential of novel urinary biomarkers to predict chronic bladder toxicity (BUSTin biomarker study being initiated)



Rodent bladder – *ex vivo* contraction assay



Lead: Karen McCloskey

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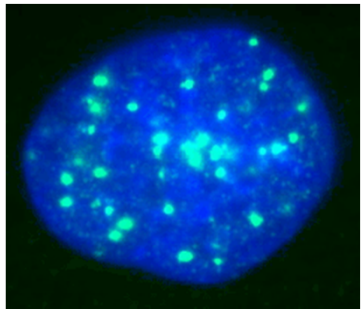
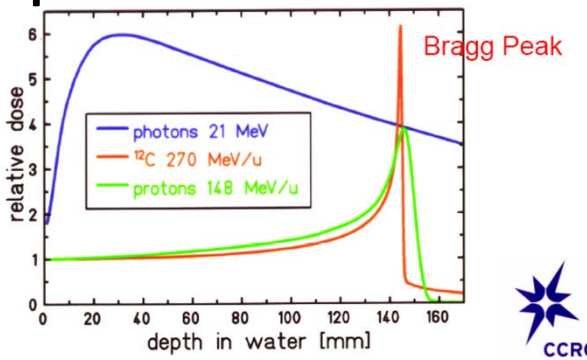
Advanced Models for Ion-beams

- Developing and future radiation-based therapies will utilise ion-beams (Protons, carbon ions)

Aims

- Optimise delivery on the basis of physical and biological mapping of the Bragg peak using experimental and clinically relevant beams
- Map lethal and non-lethal damage mechanisms in cell and tissue models to develop new biophysical models





Lead: Giuseppe Schettino

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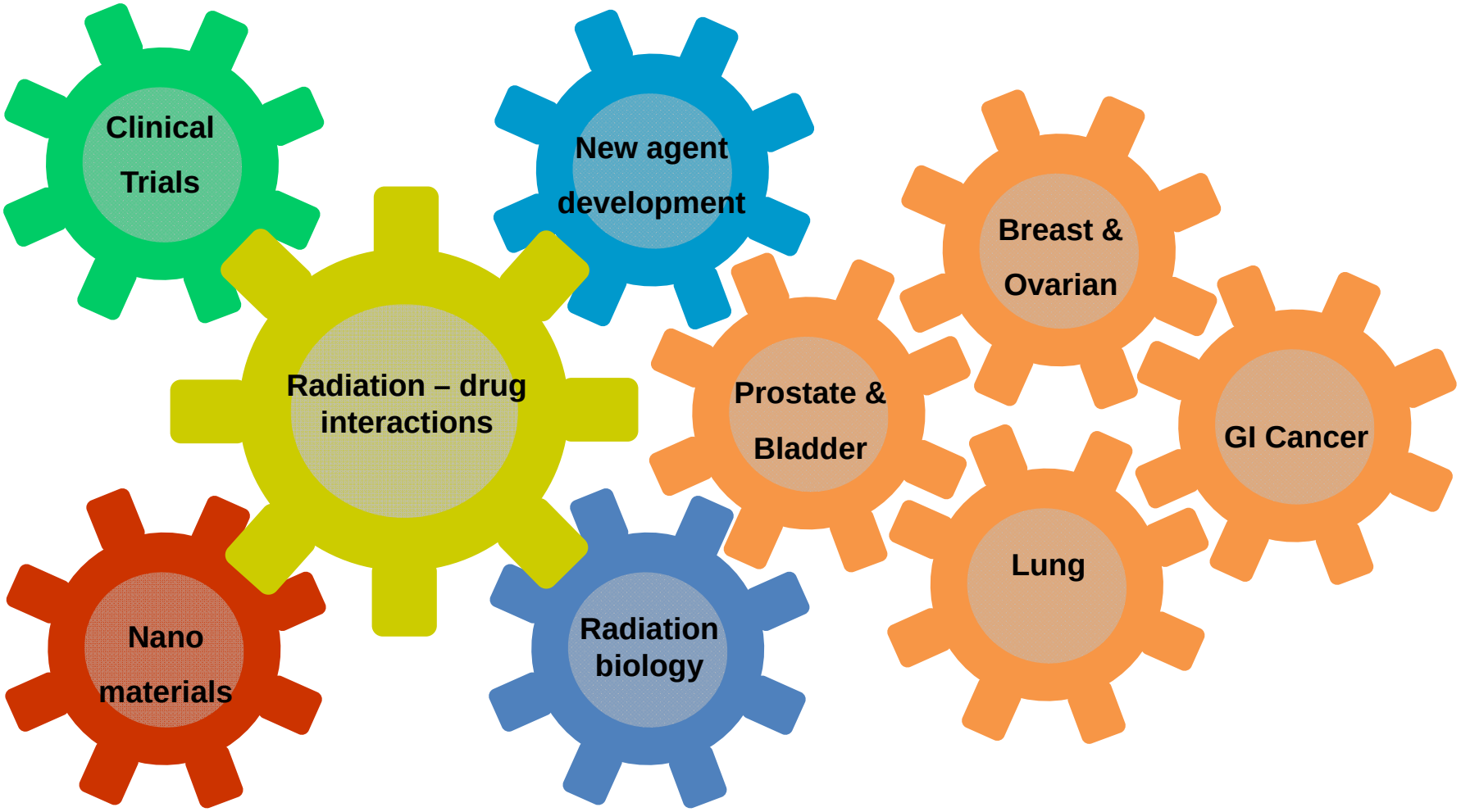
Theme 2 – Radiation-drug interactions



Gold nanoparticles
BH3 mimetics
C-FLIP inhibitors

PARP Inhibitors (+/- 5FU)
Chemokine Signalling
Radioresistance / stem cell models

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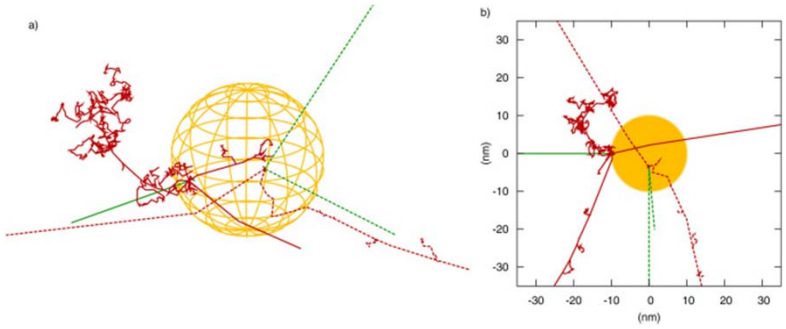
Studies with gold nanoparticles

- Gold nanoparticles hold significant potential as novel radiosensitisers and contrast agents

Aims

- Develop new biophysical models to predict their effectiveness
- Develop novel tagging strategies to target these at the tissue and subcellular levels



Lead: Fred Currell

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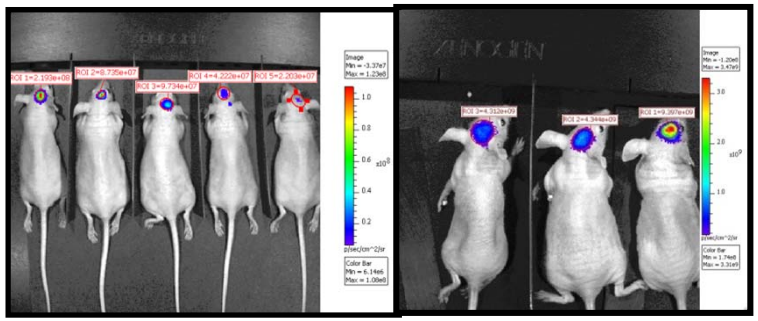
Studies in Glioma

- Optimise use of radiotherapy in glioma using new image-guided preclinical models
- Probe mechanisms underpinning radiation-induced invasion in glioma and develop drug targeting strategies including nanotechnology approaches
- Develop appropriate biomarkers for relapse and second line interventions



Lead: Tom Flannery

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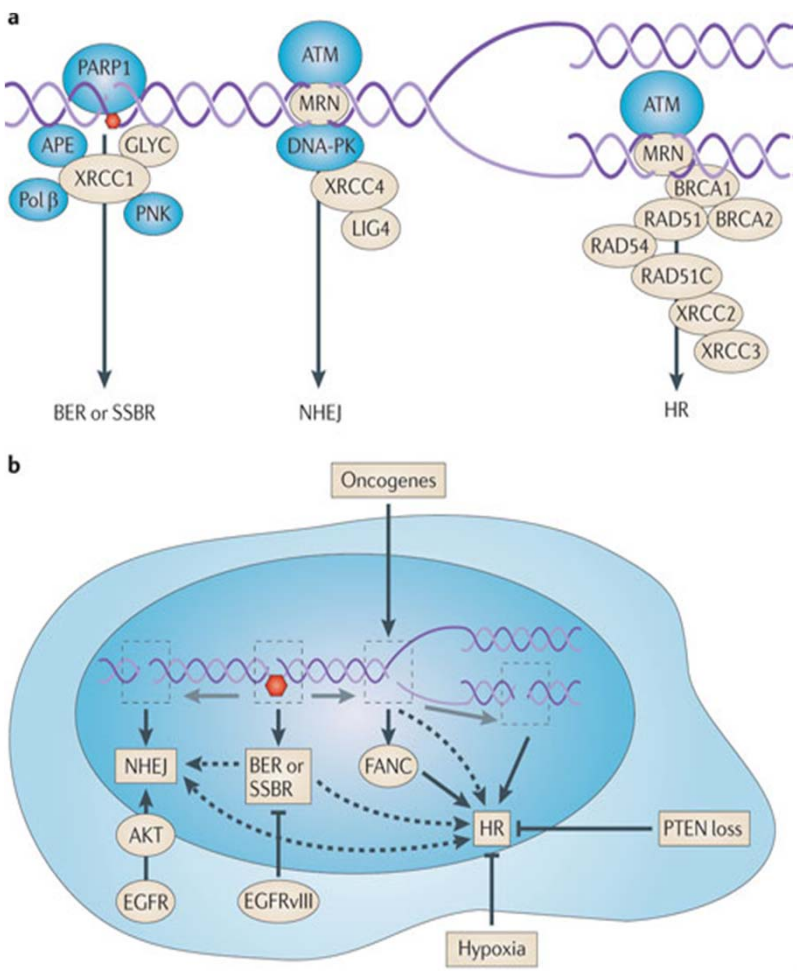
Molecular stratification in localised prostate cancer

- Key genetic events involved in the pathogenesis of prostate cancer induce or modulate the DNA damage response (e.g. PTEN, BRCA1/2)
- Optimal design and scheduling of DNA repair modulation of advanced radiotherapies will also be impacted by intercellular signalling
- Test role of beam modulation in key genetic models *in vitro* and *in vivo*
- *Feed into CCRCB Translational Prostate Program*



Leads David Waugh, Kevin Prise and Richard Kennedy

Nature Reviews | Cancer

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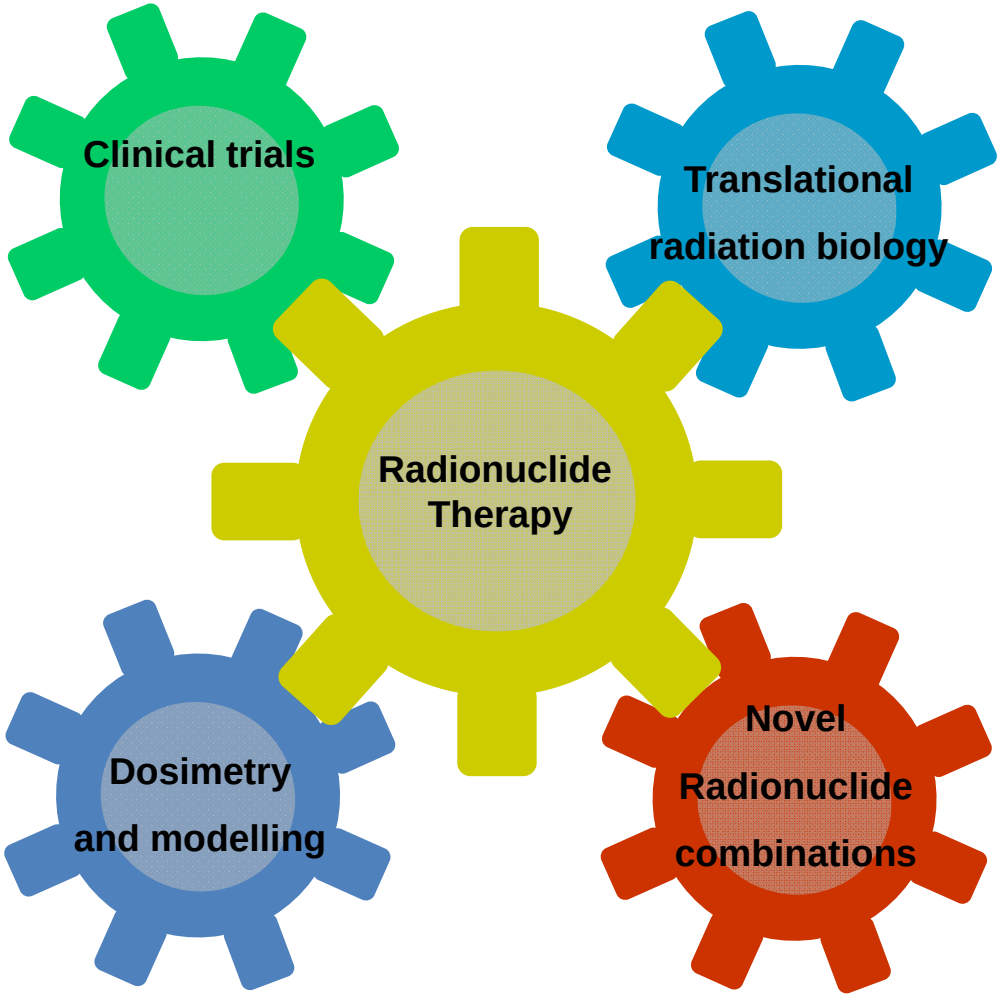
Theme 3 - Radionuclide therapy



Bone seeking radionuclides for metastasis in resistant prostate cancer

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Novel bone-seeking therapeutics

- Clinical trials with bone-seeking radionuclides have shown great promise in advanced prostate cancer trials

Aims

- Develop new agents around innovative ionic liquid and phosphate chemistry
- Design optimal strategies of diagnostic/ therapeutic response to be tested in preclinical models

Lead: Marie Migaud

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