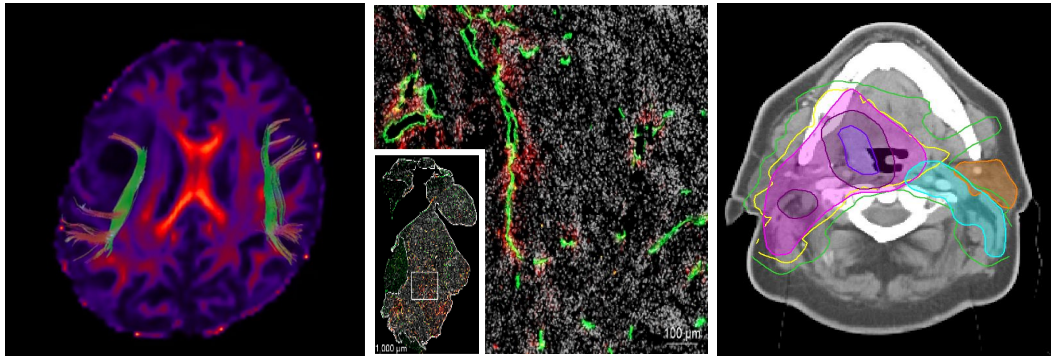


Ymchwil Iechyd a Gofal Cymru
Health and Care Research Wales

Developments in Cancer research

– viruses, vaccines and radiotherapy

Health and Care Research Wales conference 2021

Mererid Evans

14 October 2021

GIG CYMRU NHS WALES
Ymddiriedolaeth GIG Prifysgol Felindre Velindre University NHS Trust

Canolfan Ymchwil Canser Cymru
Wales Cancer Research Centre

CARDIFF UNIVERSITY
PRIFYSGOL CAERDYDD

Cancer- causing viruses

- **Viruses cause ~15% of the global cancer burden**

- 1911 Peyton Rous
  - cell free transmission of sarcoma

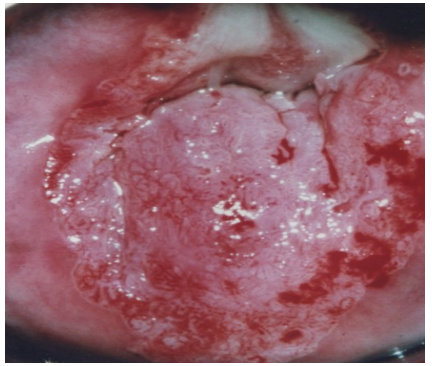
- 1964 Anthony Epstein & Yvonne Barr
  - discovered Epstein Barr virus (EBV) virus in Burkitt's lymphoma

- 1983 Harald zur Hausen
  - isolated HPV16 from cervical cancer

- Others include Hepatitis B and C (Liver cancer)

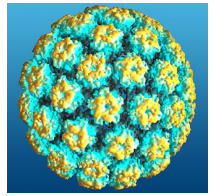
- **Cancer usually occurs years or even decades after primary infection**

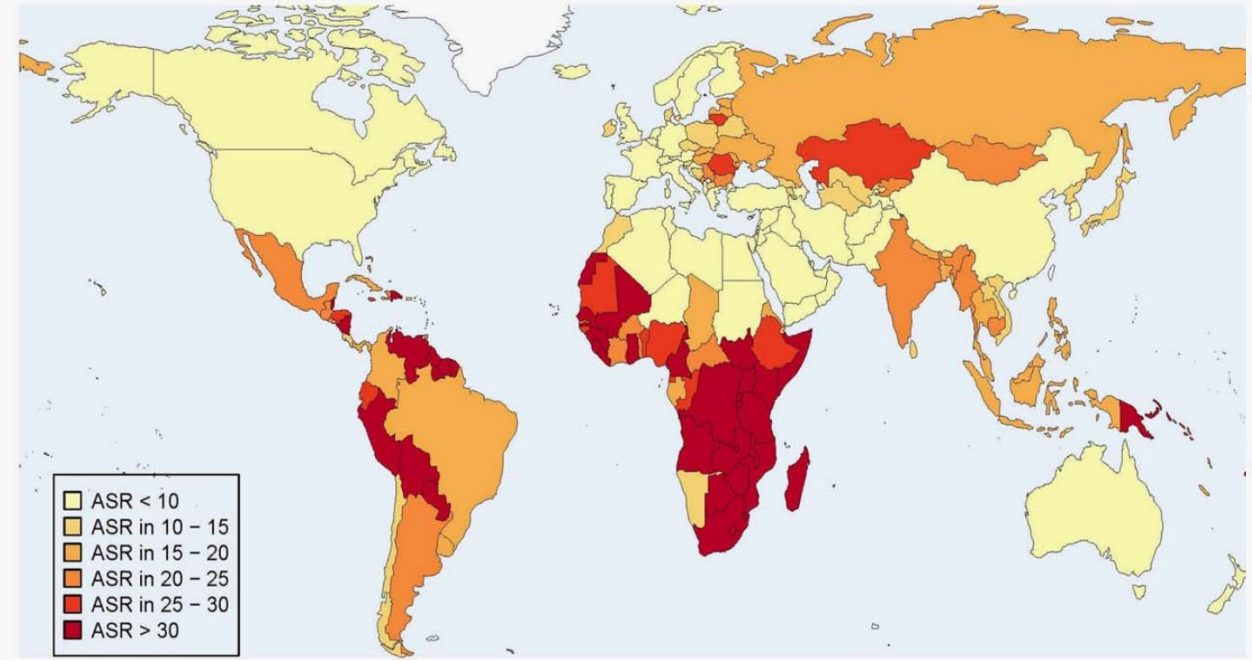
Francis Peyton Rous
Nobel prize (Medicine) 1966



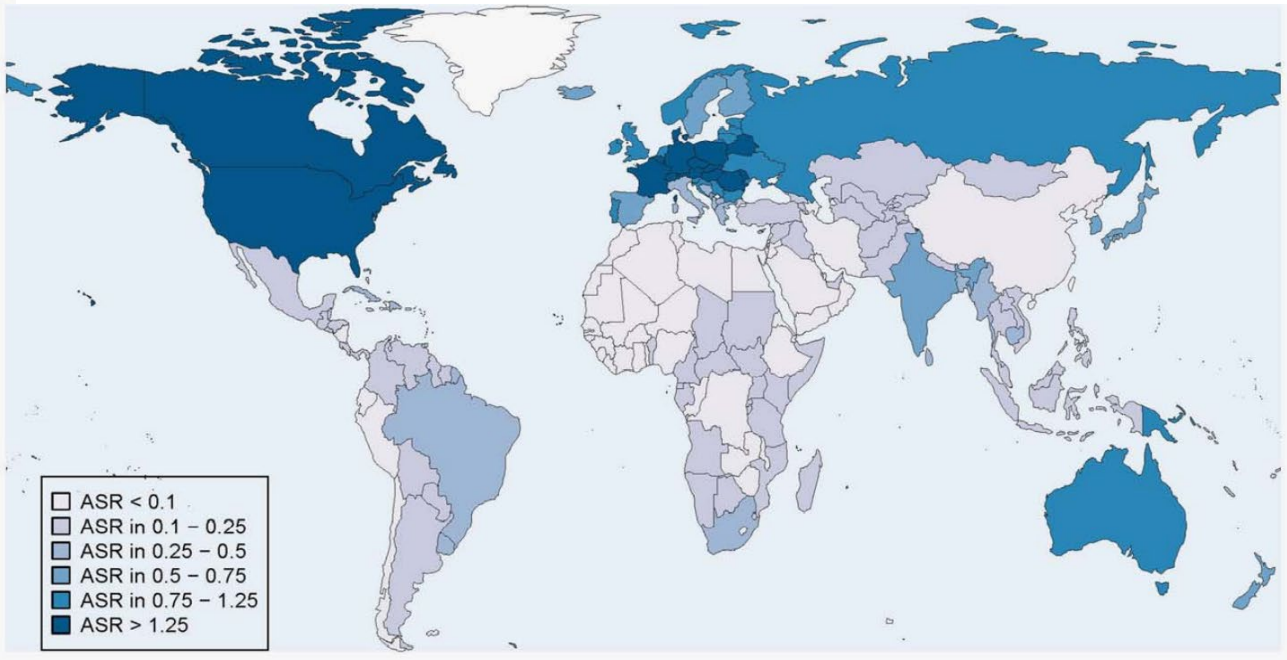
Harald zur Hausen
Nobel prize (Medicine) 2008

HPV – a significant cause of cancer worldwide

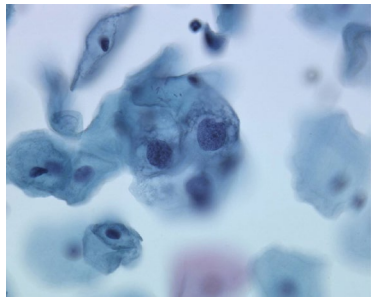




Age standardised incidence rates (per 100,000) of cervical cancer attributable to HPV



Age standardised incidence rates (per 100,000) of head & neck cancers attributable to HPV



screening

vaccination

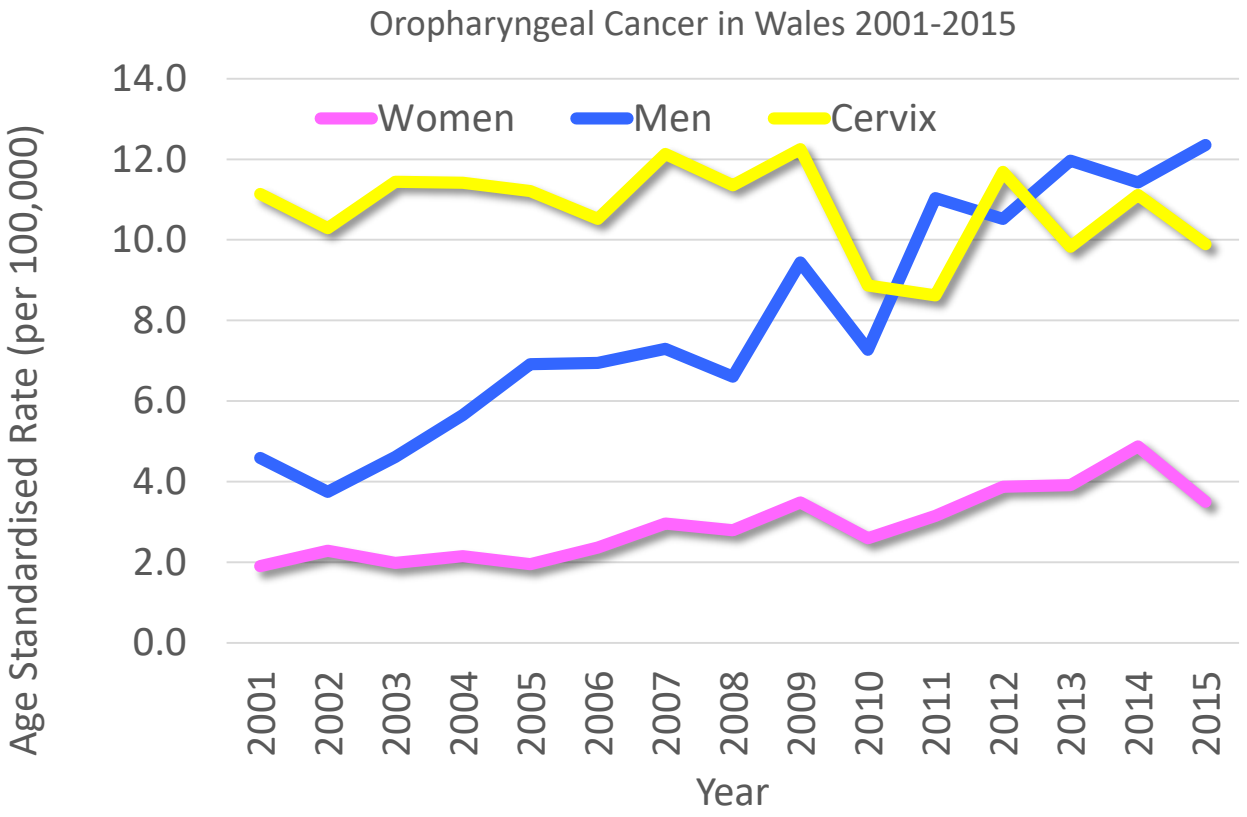
HPV-associated head and neck cancer: a virus-related cancer epidemic

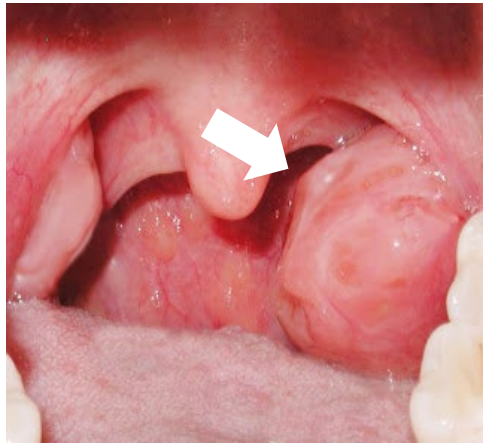
Shanthi Marur, Gypsyamber D'Souza, William H Westra, Arlene A Forastiere

Lancet Oncology

[Martel *et al*, International Journal of Cancer 2017]

The “HPV Throat Cancer Epidemic” in Wales

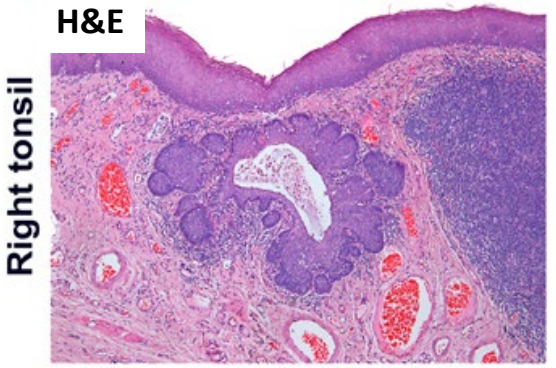


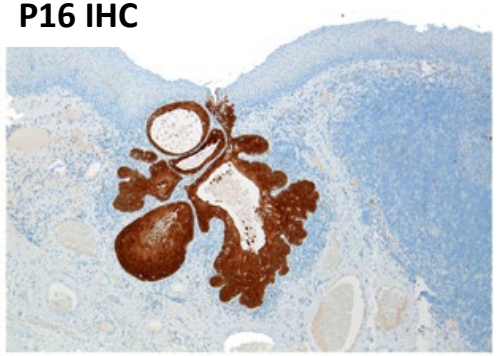


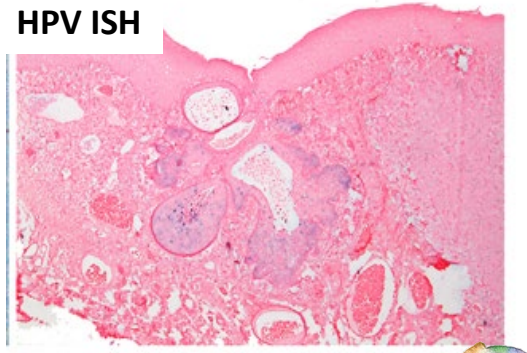
Left tonsil cancer

55-80% positive for HPV

Pathology blocks tested for HPV GP5+/6+ PCR, ISH and p16 IHC

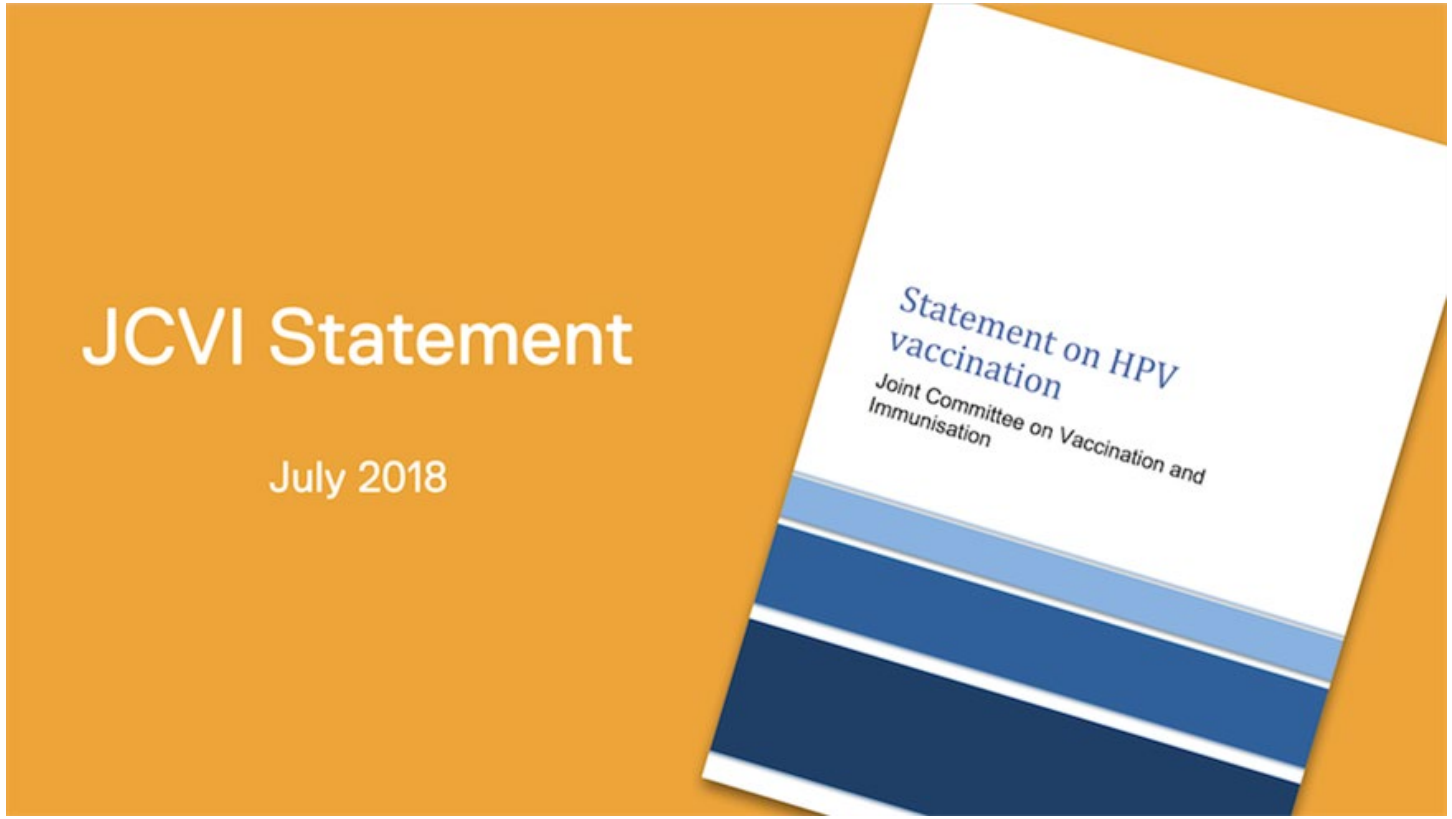






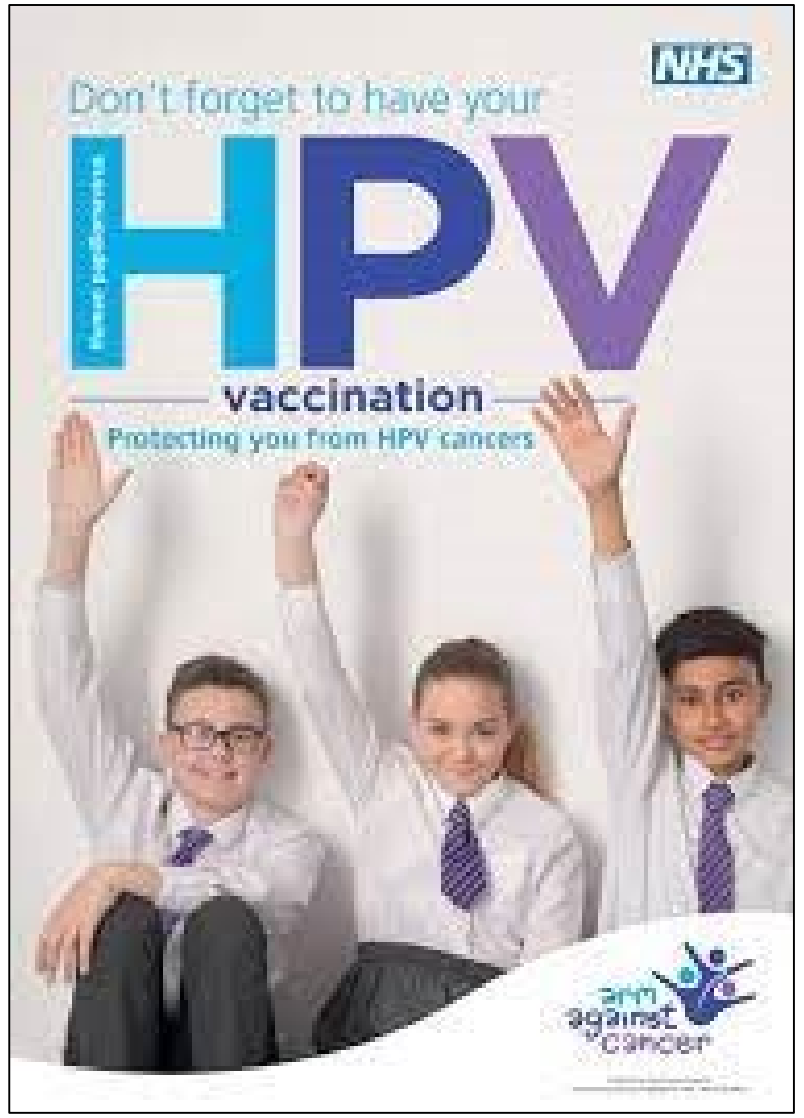
Source: Welsh Cancer Intelligence and Surveillance Unit, Health Intelligence Division, Public Health Wales

CANCERRESEARCHWALES
YMCHWILCANSERCYMRU

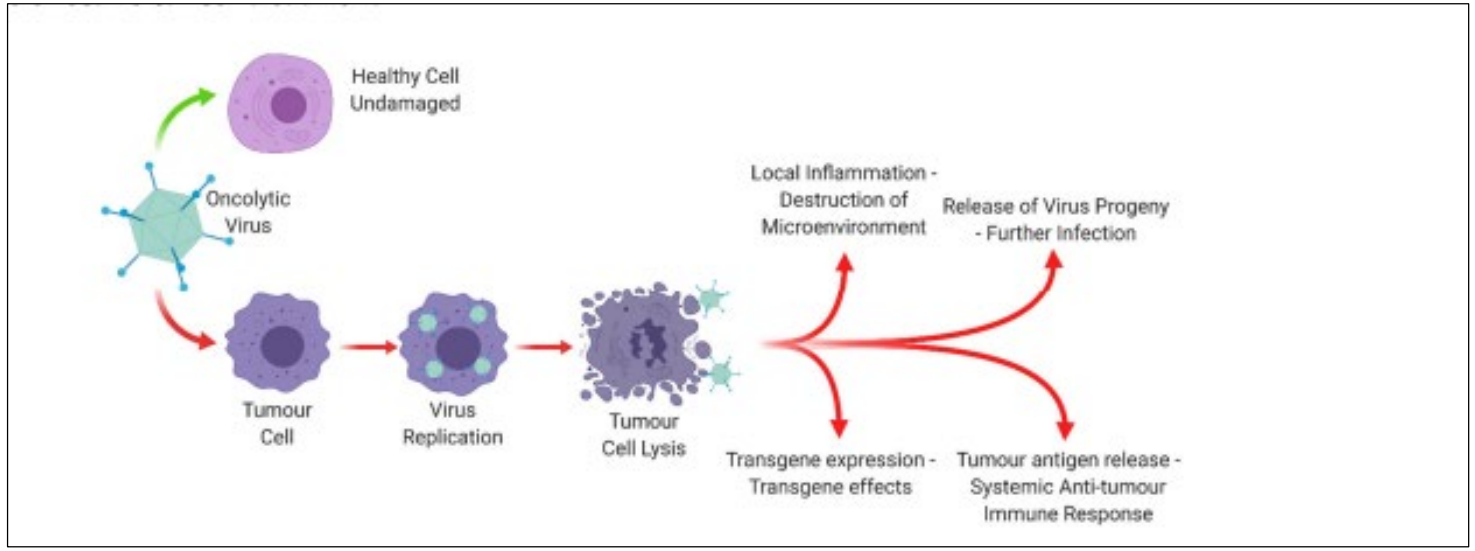


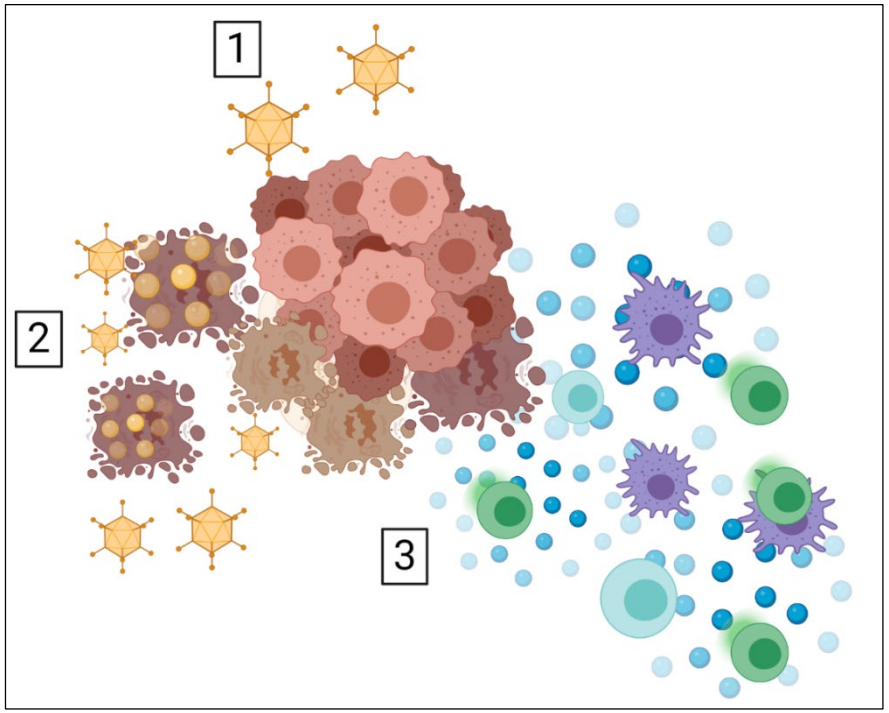
Our work in Wales informed the JCVI advice to extend **UK HPV vaccination programme** to include boys (07/2018), preventing future cancers.

[Evans, Powell *et al*. *BMC Cancer* 2013; Schache, Powell, Evans *et al Cancer Res* 2016]



Cancer vaccines – promise for the future





1. Tumour selective Oncolytic virus
2. Virus infects tumour cell which dies
3. Immune response

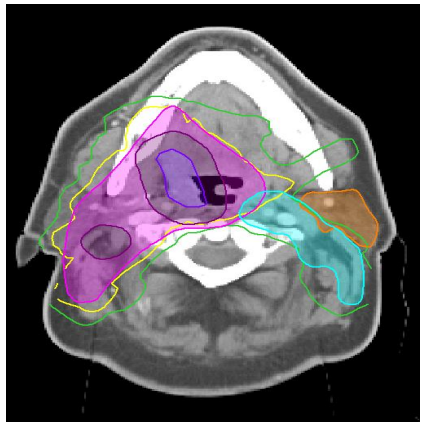
Prof Alan Parker

UK Lifesciences vision 2021: Healthcare Mission “enabling immune therapies such as cancer vaccines”

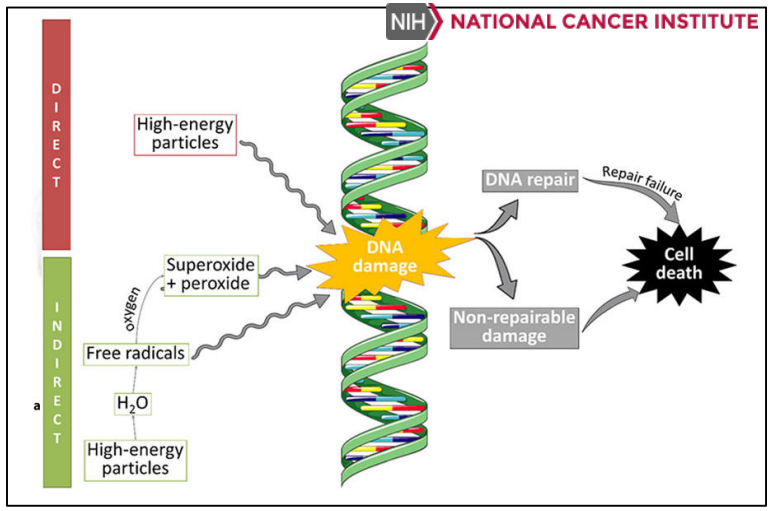
A good time to be involved in cancer research in Wales

- CReSt themes:
  - Precision and mechanistic oncology
  - Immuno-oncology
  - Radiotherapy
  - Cancer clinical trials, including experimental therapeutics
  - Supportive and palliative oncology
  - Cancer prevention, early diagnosis, primary care and health service research

Linear Accelerator – produces X-Rays



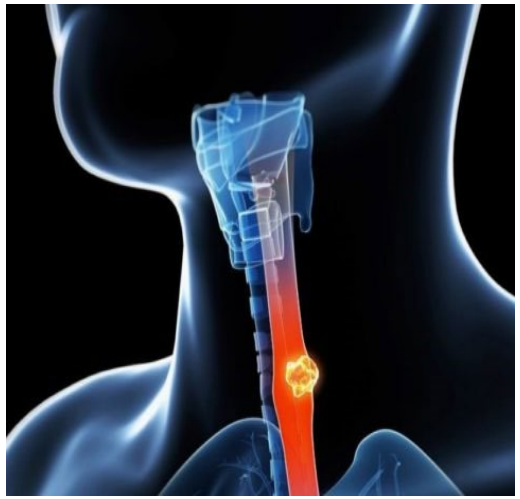
Targeted at a cancer (in the tonsil)



Causes DNA damage which (if not repaired) leads to cell death

Wales - leading clinical radiotherapy research in different cancers

Upper Gastrointestinal



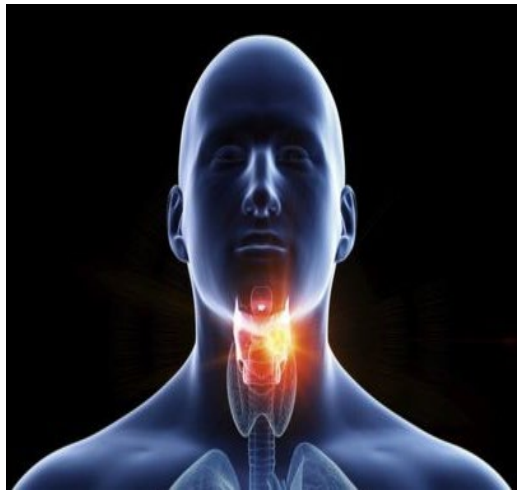
SCOPE

NeoSCOPE

OCCAMS

Oesophageal Cancer Clinical and Molecular Stratification

Head & Neck cancer



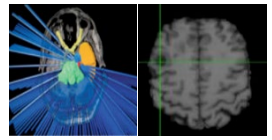
Pathos

PEARL

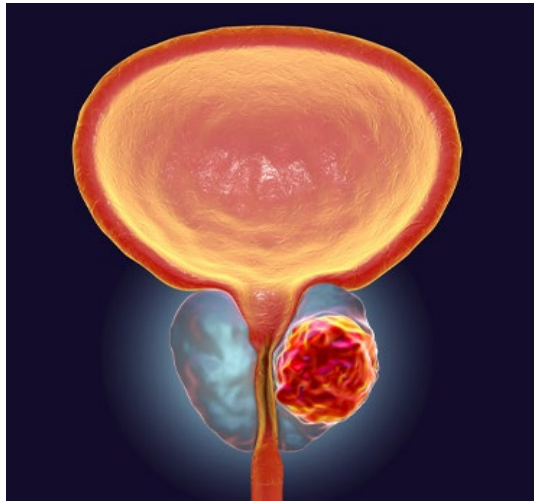
POSITIVE

Brain cancer

Neurocognitive Function Study



Prostate cancer



Wales is 1 of 4 UK RTTQA centres – ensuring the best radiotherapy is delivered to patients every time

NCRI Advancing Cancer Research Together

RTTQA

Radiotherapy Trials Quality Assurance

Pathos

Phase 3 Randomised Controlled Trial

HPV positive head & neck cancer

Minimally invasive surgery (laser or robot)

Pathology assessment

- Low risk → A → No post-operative treatment
- Intermediate risk → Randomise → B
  - B1 **Radiotherapy** – standard dose (control)
  - B2 **Radiotherapy** – low dose (test)
- High risk → Randomise → C
  - C1 **Radiotherapy** + Chemotherapy (control)
  - C2 **Radiotherapy** only (test)

ITV REPORT 13 February 2019 at 6:00am

£2 million funding boost for head and neck cancer research in Cardiff

The research aims to find kinder treatments for patients.

A Cardiff researcher has received a £2.15 million grant from Cancer Research UK to help fund the discovery of kinder treatments for head and neck cancer patients.

The aim of the study is to reduce the intensity of head and neck cancer treatment. Current treatments can result in "devastating" side-effects for some patients – including losing the ability to swallow.

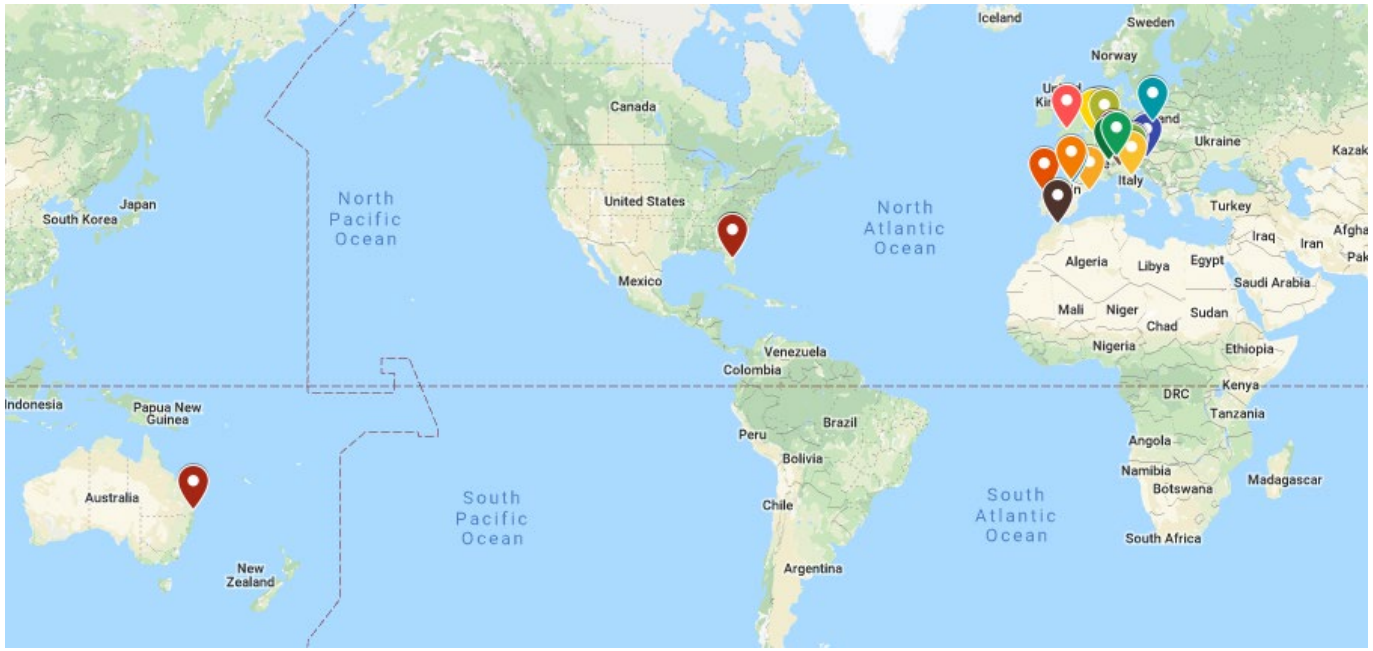
Co-primary endpoints: swallowing function and Overall Survival

"Developing kinder treatments for patients with head and neck cancer"

PATHOS – UK & International

584 patients recruited
by 11 Oct 2021
(target 1100 patients by Oct 2023)

Open in **36 UK sites**

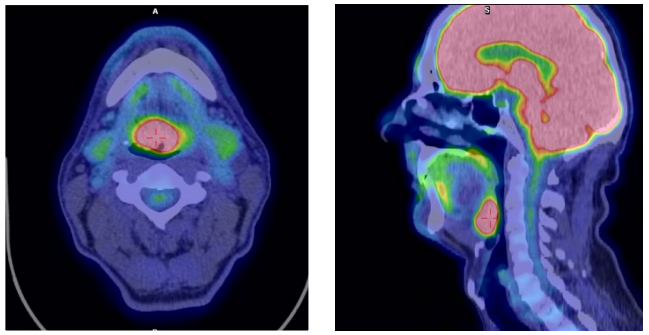


Open in **8 international sites** (**USA** [Florida, Stanford**], Australia** [Brisbane], 6 in **France**).
In **set-up in 18 international sites** (5 in France, 10 in **Germany**, 2 in **Switzerland** and 1 in **Hong Kong).**

Could establish a new international standard of care for the treatment of HPV-positive head & neck cancer

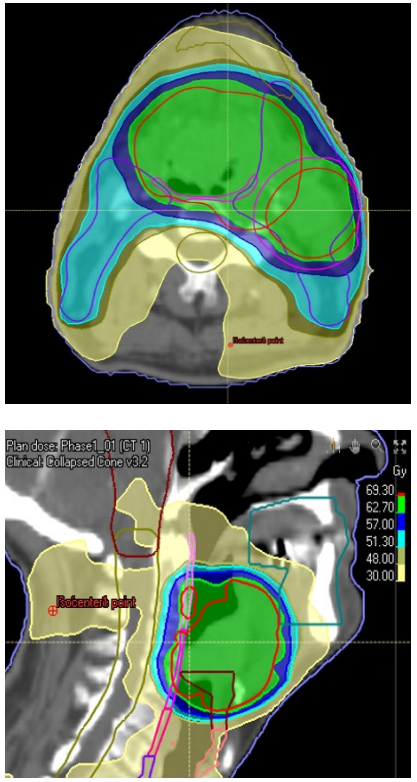
"Developing kinder treatments for patients with head and neck cancer"

PEARL: PET based Adaptive RT TriaL



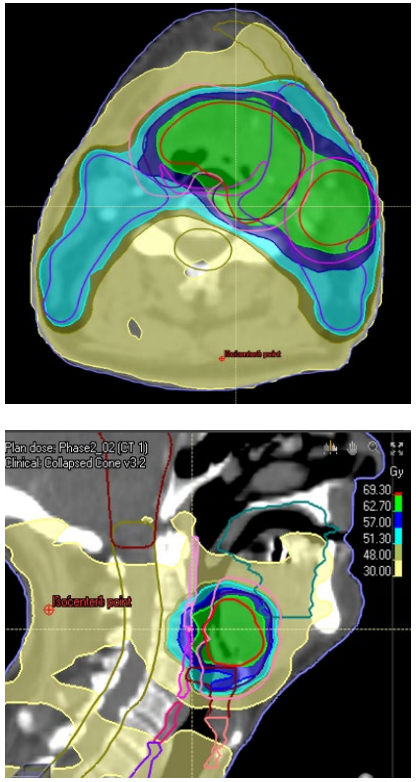
Tongue base cancer seen on FDG-PET-CT scan

Week 1-3 of radiotherapy



Plan based on PET-active cancer at baseline

Weeks 4-6 of radiotherapy



Adapted plan based on biological response

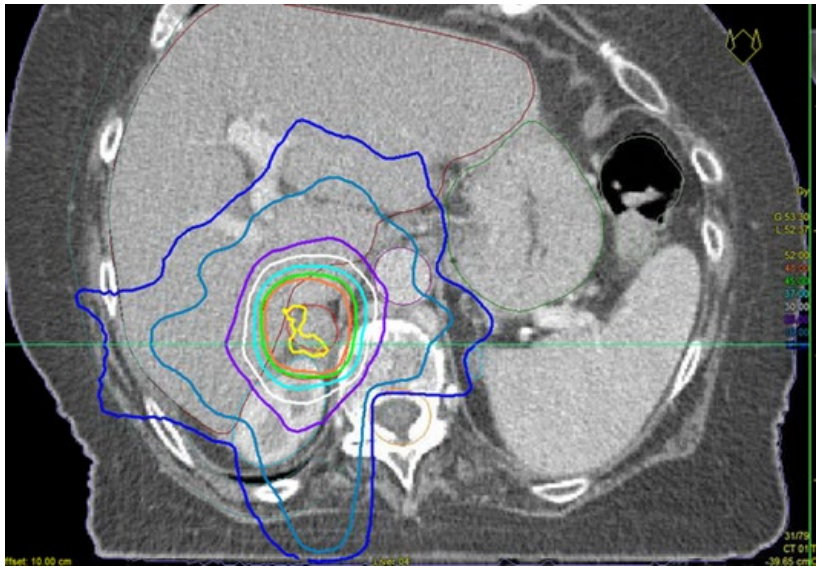
Aim: to reduce high dose treatment volume in responding patients to reduce toxicity

Co-CI: Dr T Rackley, HCRW Clinical Research Time Awardee

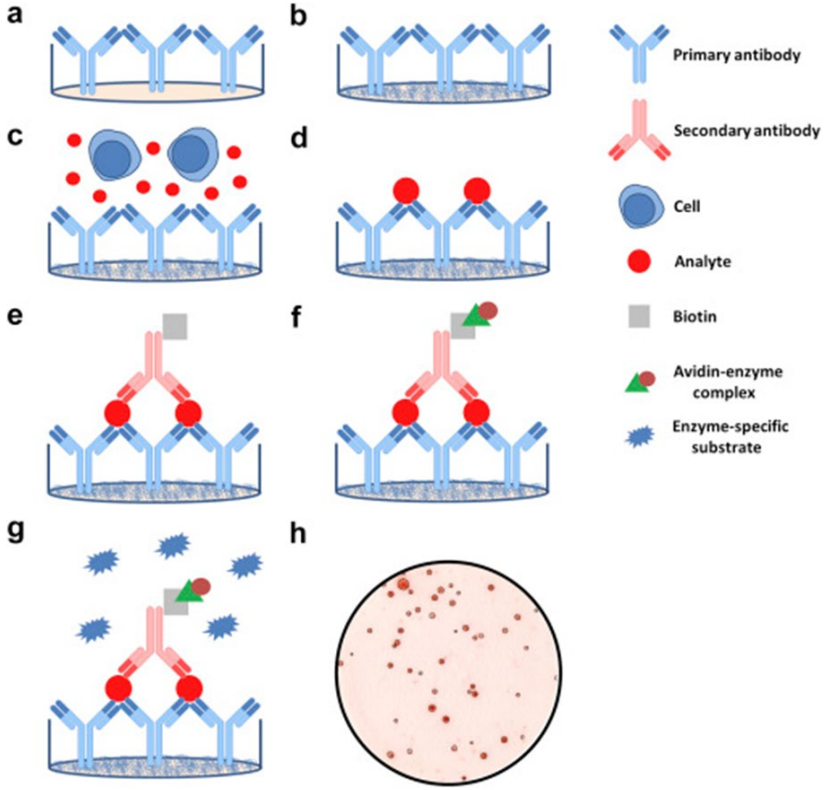
“Developing kinder treatments for patients with head and neck cancer”

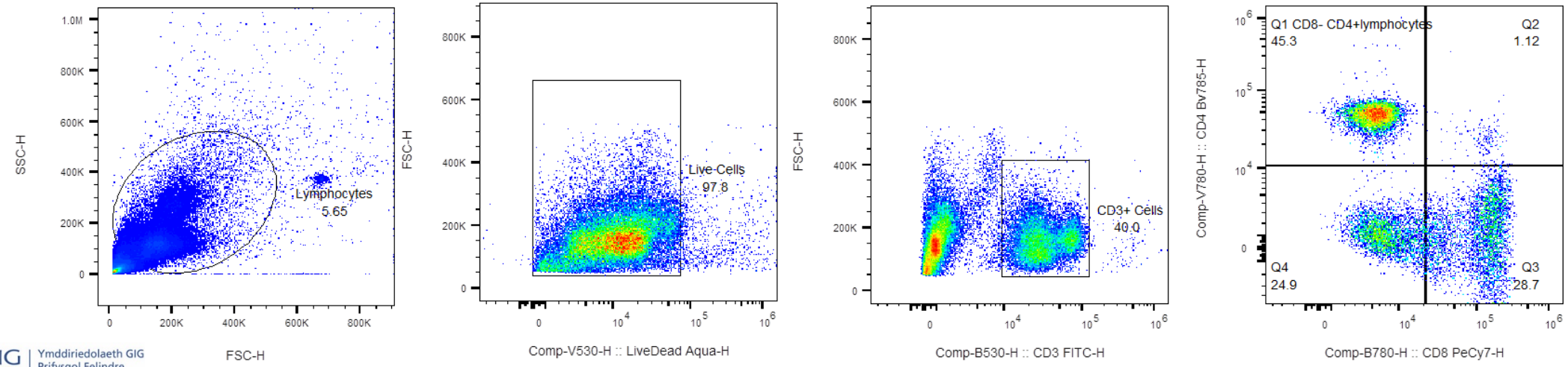
SABR_IT Study

[Awen Gallimore, Andy Godkin, Tom Rackley, Cath Pembroke]



- Blood taken at 5 time points (before, during and after RT and at recurrence)
- Enzyme-linked immunospot (ELISPOT) assay
- Flow Cytometry



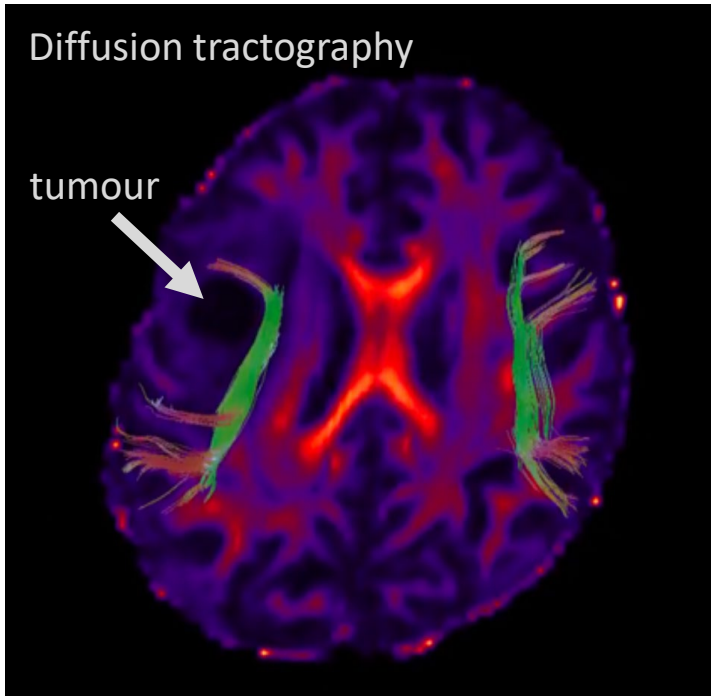


Slide courtesy of Dr Tom Rackley

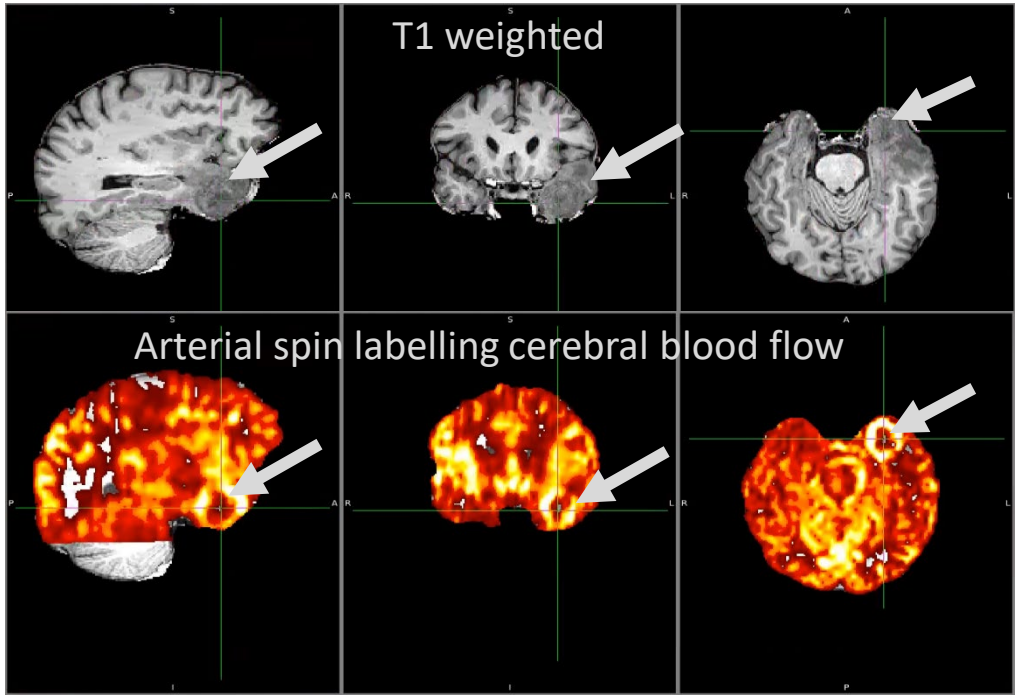
Neurocognitive function study

[James Powell, Sahar Iqbal, Richard Wise]

40 patients with brain oligo-metastases, mpMRI pre and post Stereotactic Radiosurgery (SRS)



Superior Longitudinal fasiculus tract (green) displaced medially



Orange/yellow = high blood flow. Tumour core has low blood flow [associated with poor outcome], with a high flow border.

Radiotherapy

Data, Automation and AI

Using AI to select cancers for RT & automation to improve efficacy

SPAARC
Spaarc Pipeline con Automated Analysis and Radiomics Computing

TLAAS
Automatic decision Tree Algorithm for Advanced Segmentation

IBSI
image biomarker standardisation initiative

ESGAR 2018 Silver prize best paper

IPEM
Institute of Physics and Engineering in Medicine
IPEM 2015 Manufacturer's Award for Innovation

ESTRO
ESTRO 2016 Best Physics poster award

RTTQA
Radiotherapy Trials Quality Assurance

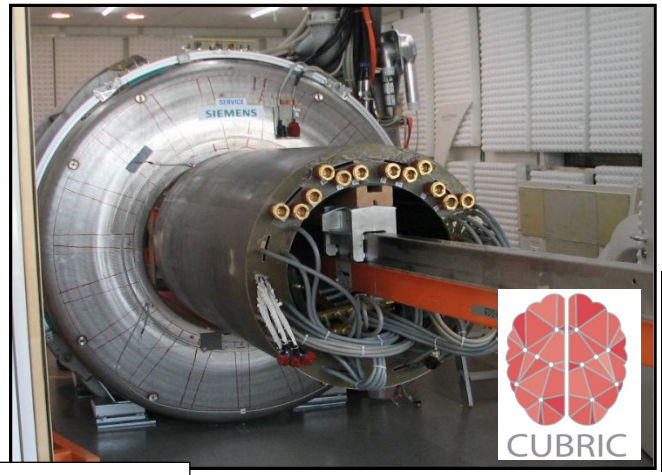
ASPIRE: AI Solutions for Personalised RadiothErapy
1.1k 3D scans
12k labeled images
Anatomical and Functional information

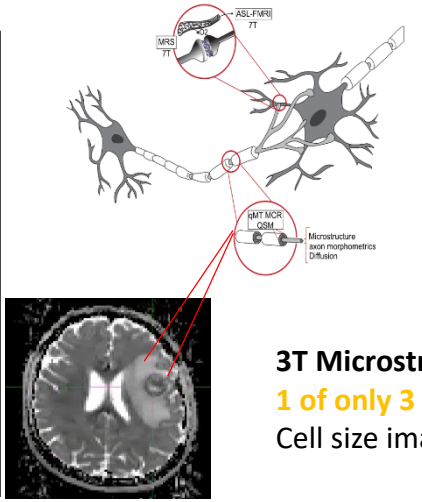
EdgeVCC
Automated RT planning

→ Innovation

Imaging

Using world-class imaging to understand the microstructural & biological effects of radiotherapy

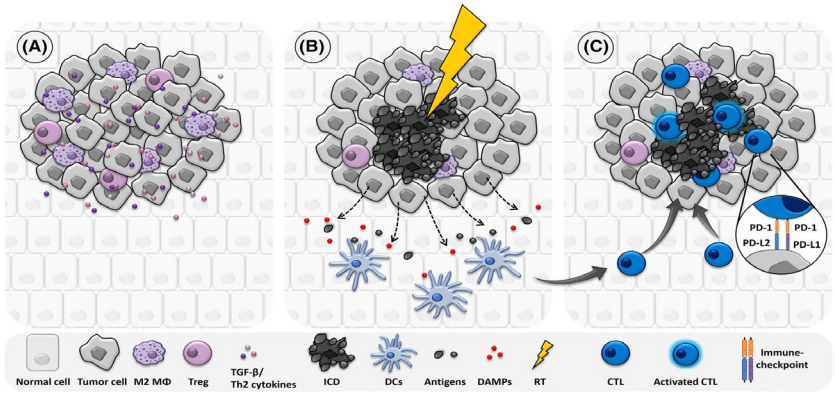




3T Microstructural MRI
1 of only 3 in the world
Cell size imaging

Immunology

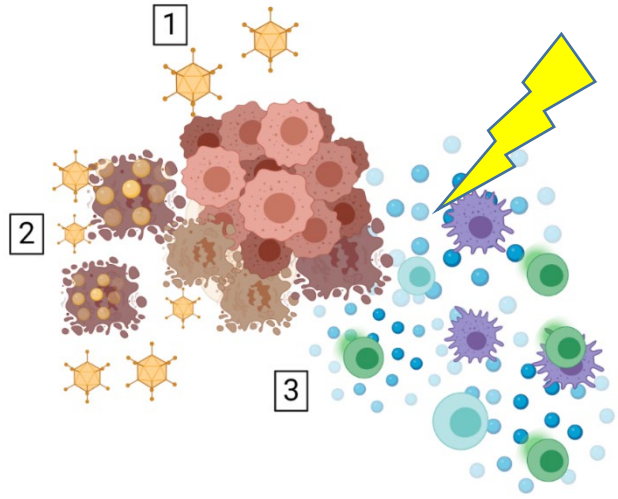
Turning immunologically 'cold' tumours into 'hot' tumours with radiotherapy



[Ruckert *et al*, Stem Cells 2021]

Novel agents including Cancer Vaccines

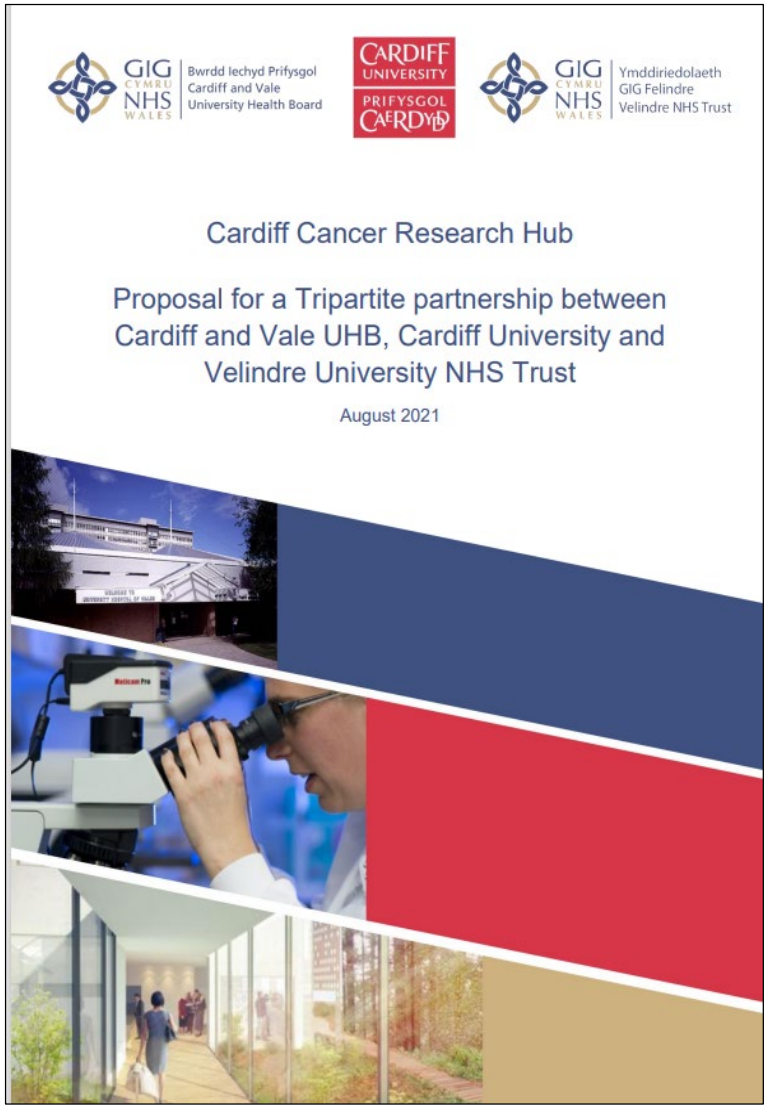
Combining RT with tumour selective oncolytic viruses = radioimmunovirotherapies



[Courtesy of Prof Alan Parker]

ECMC
CARDIFF UNIVERSITY
PRIFYSGOL CAERDYDD

Developing new infrastructure for research in Wales



- **Increasing patient access to research** - including Early Phase Trials (EPTs) and Advanced Therapies for solid cancer and haemato-oncology
- **Strengthening the translational pipeline** → enabling scientists to bring new discoveries through to the clinic & encouraging new scientific discovery
- **Developing a focus for cancer research excellence** in Wales → enhancing reputation and attracting future funding, partners & staff
- **Enabling training, education & innovation**
- Housing **Welsh research infrastructure**, hub for **industrial partnerships**.

Strongly supported by Cardiff & Vale University Health Board & Velindre University NHS Trust Partnership Board with Cardiff University 3rd August 2021

ECMC

Priorities for Cancer Research in Wales

- Build a sustainable, internationally competitive portfolio of cancer research in Wales, **focused on thematic areas of research excellence** where Wales can make a unique or significant contribution and build critical mass
- Work together as a '**One Wales'** team of researchers, across different institutions, disciplines & diverse skills
- Look outwards to establish effective research partnerships and networks **across the UK and internationally**
- Enable the **translational pipeline** between the laboratory and clinic → developing new infrastructure and people
- Inspire and establish career pathways for **future research leaders** → Clinical, Academic and Clinical Academic.

Canolfan Ymchwil Canser Cymru
Wales Cancer Research Centre

What we can achieve….

- A thriving, connected cancer **research community** in Wales
- An **identity**, **focus & enhanced reputation** for cancer research in Wales
- **Inward investment**, ensuring sustainability and benefitting the Welsh economy
- A positive legacy to hand onto the **next generation** of researchers & cancer patients in Wales
- **Health benefits** for cancer patients and the public **across the whole of Wales**

→ Realising these benefits is a collective endeavour (individual, institutional, governmental…)

The Wales Cancer Research Centre

- WCRC is an **established & valued** part of the cancer research infrastructure in Wales which makes people feel part of something bigger. It is a vehicle to:

  - Influence a harnessed approach for a joined up '**One Wales**' for cancer research
  - Realise opportunities to develop **new infrastructure** to benefit cancer research & patients in Wales
  - Champion the cancer research **workforce** in Wales which needs urgent investment & development of career pathways to build critical mass & a thriving cancer research community for the future
  - Promote and drive the implementation of **CReSt** for patients and researchers in Wales, working closely with HCRW and with institutions across Wales to ensure its success.

Canolfan Ymchwil Canser Cymru
Wales Cancer Research Centre

Ymchwil Iechyd a Gofal Cymru
Health and Care Research Wales

Thank you-Diolch yn fawr