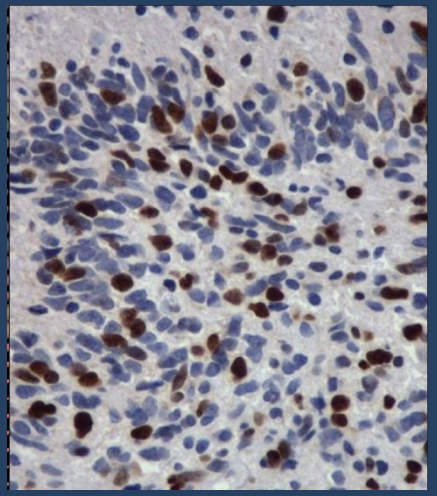
PhD SUMMER SCHOOL

Pixel Perfect

Dr Raj Jena: Advancing Computer Image Analysis to Improve Clinical Outcomes



University of Cambridge
Department of Oncology

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Science & Technologies Facilities Council

Royal College of Radiologists

EU FP7

National Cancer Intelligence Network

CERN

University of Surrey

OVERVIEW

Computational imaging | a definition

Glioblastoma | the burden of disease

Imaging tumour phenotype

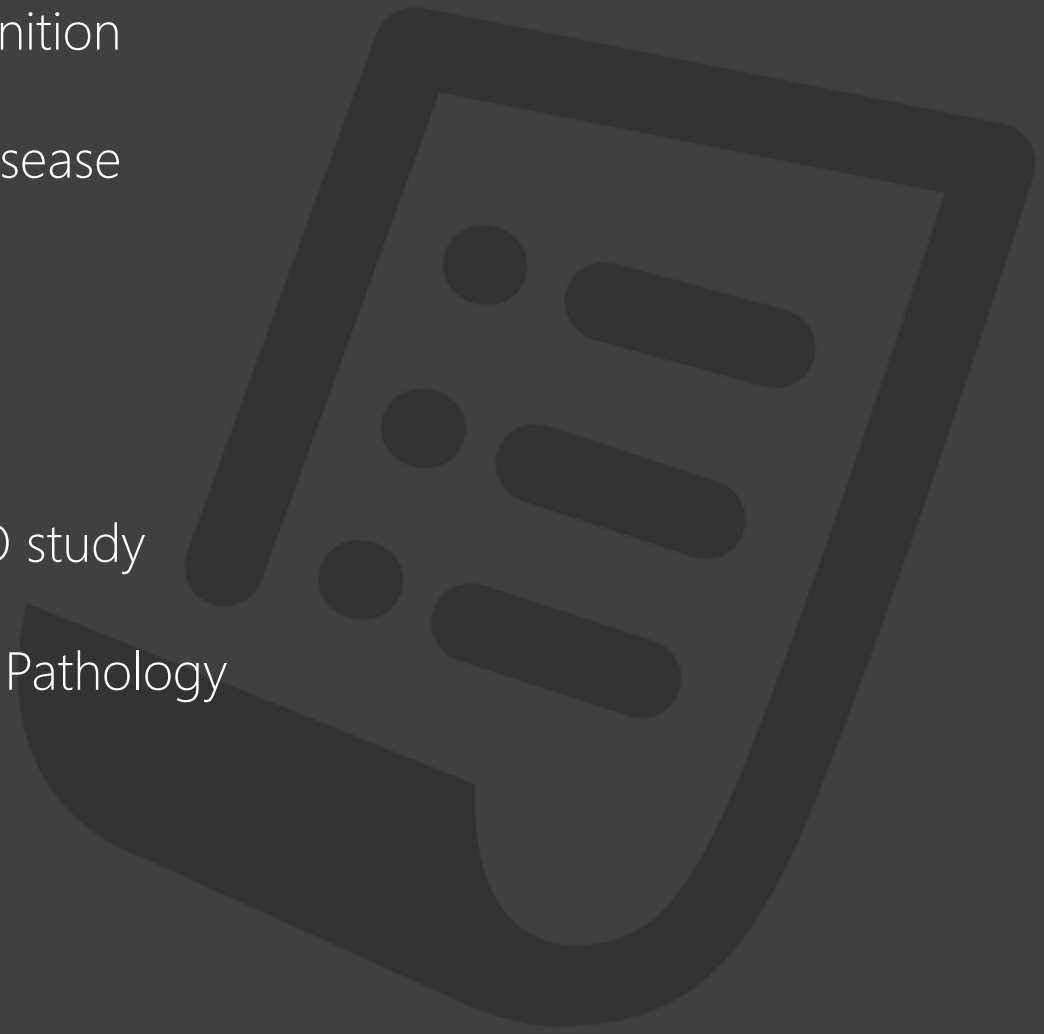
DTI | my story

Theory into practice | The GIRO study

From patients to cells | Tumour Pathology

What lies ahead

Thoughts and Conclusions

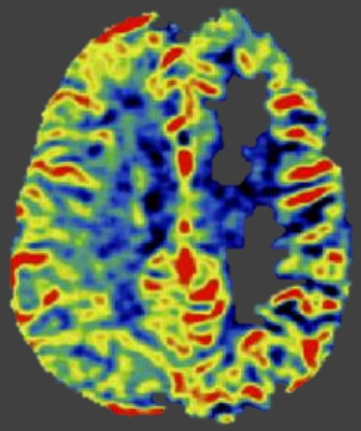


Computation is used to generate all forms of digital images

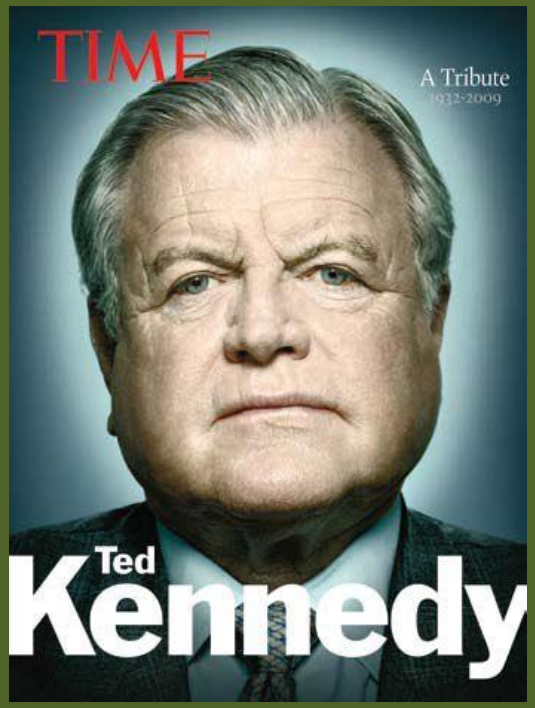
Computational imaging refers to additional processing of raw image data to provide quantitative information.

May involve encoding quantitative data into some form of model

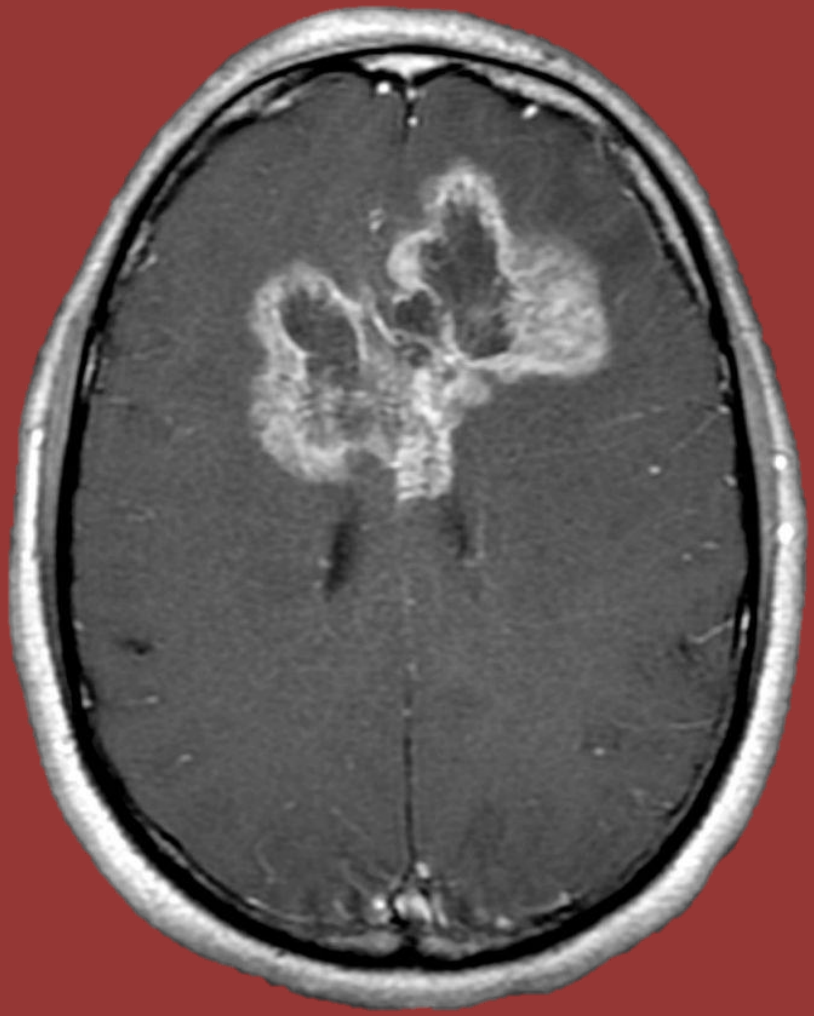
- Model encodes understanding
- Model can be validated against observation

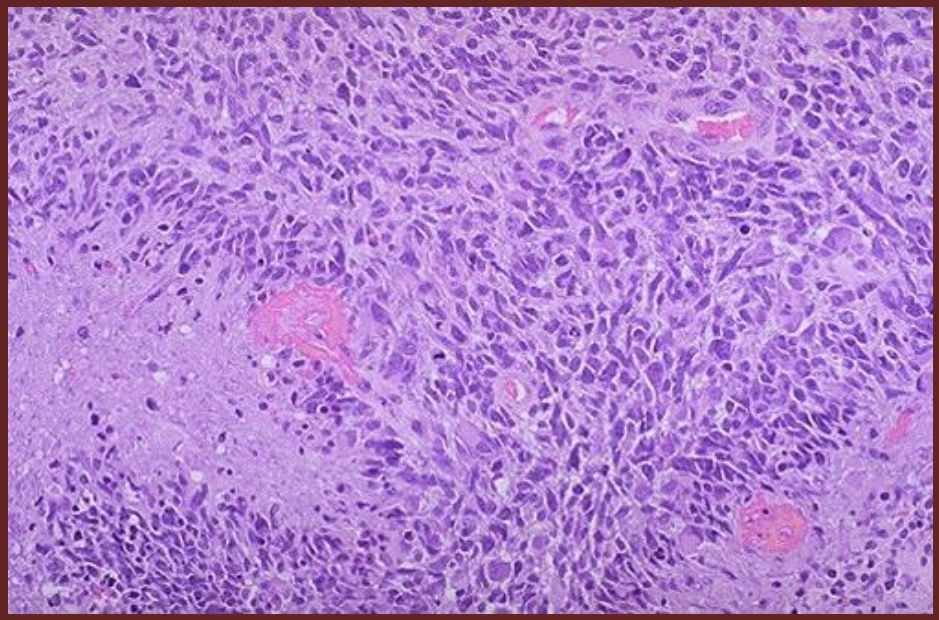


What links these gifted people?



A disease responsible for **more years of life lost** per patient than any other common adult cancer …

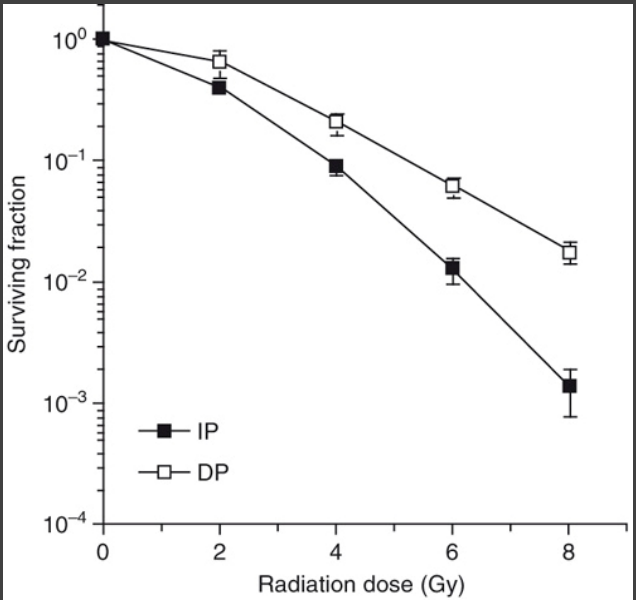




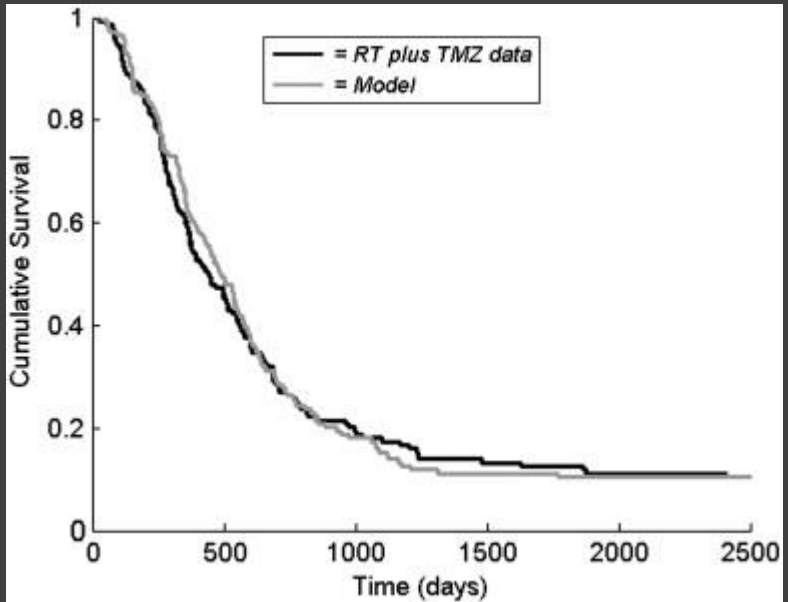
Glioblastoma

Highly heterogeneous tumour, at macroscopic and microscopic level

Tumour spread along white matter tracts



Franken at al, Clonogenic assay of cells in vitro Nature Protocols 1, 2315 - 2319 (2006)



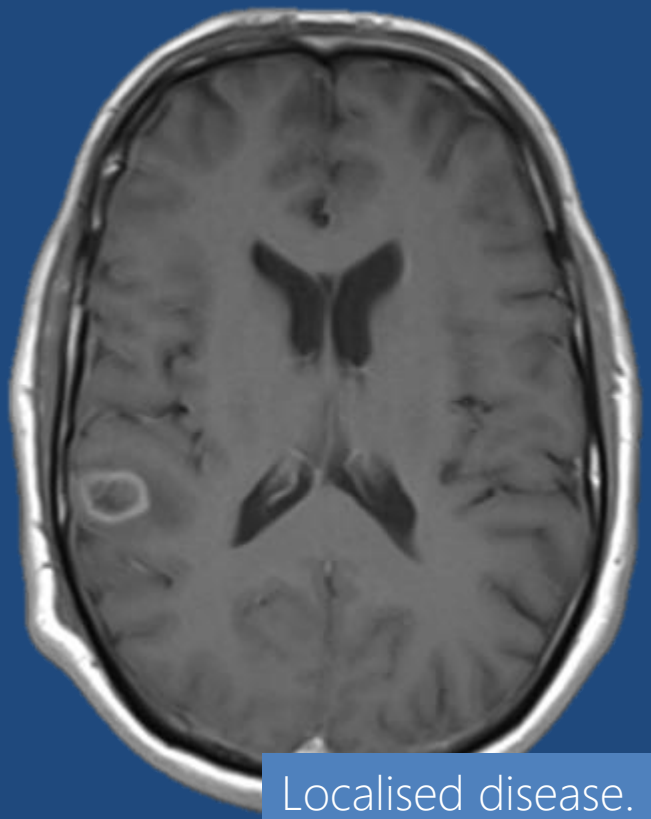
Kirkby NF , Jefferies SJ, Jena R , Burnet NG. A mathematical model of the treatment and survival of patients with high-grade brain tumours. JTB 245(1) 2007, P.112–124

Tumour infiltration

Spread into surrounding brain tissue at low density

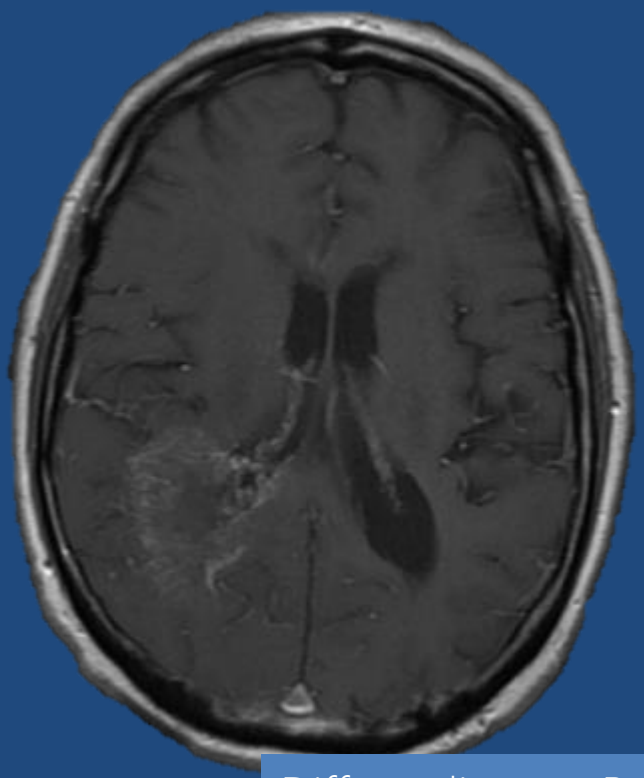
Toxicity of radiotherapy to normal tissues limits our ability to sterilise tumour

Minimally invasive phenotype



Localised disease. Most suitable for RT dose intensification

Infiltrative phenotype



Diffuse disease. Best suited to a systemic therapy

SEGUE

A splendid dinner at a Cambridge College

Gives me my first exposure to computational imaging …

DIFFUSION TENSOR IMAGING | WHITE MATTER LAID BARE

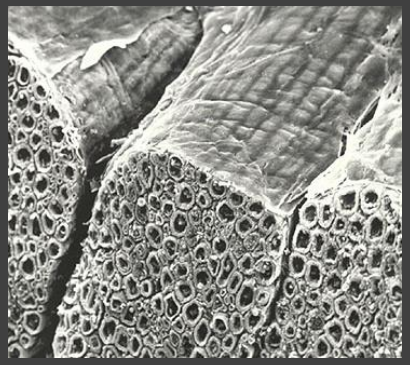
DIFFUSION TENSOR IMAGING | HOW IT WORKS

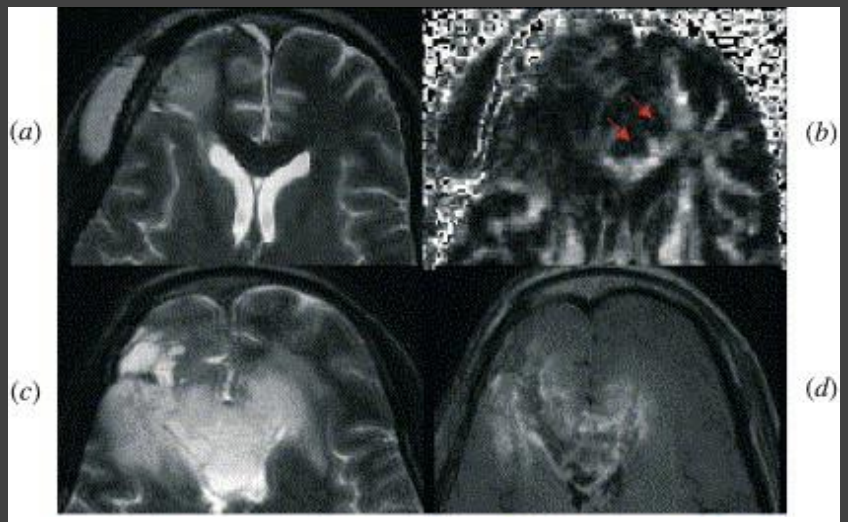
Novel technique for studying pathology of white matter tracts

Based on detecting water diffusion pattern along white matter fibres

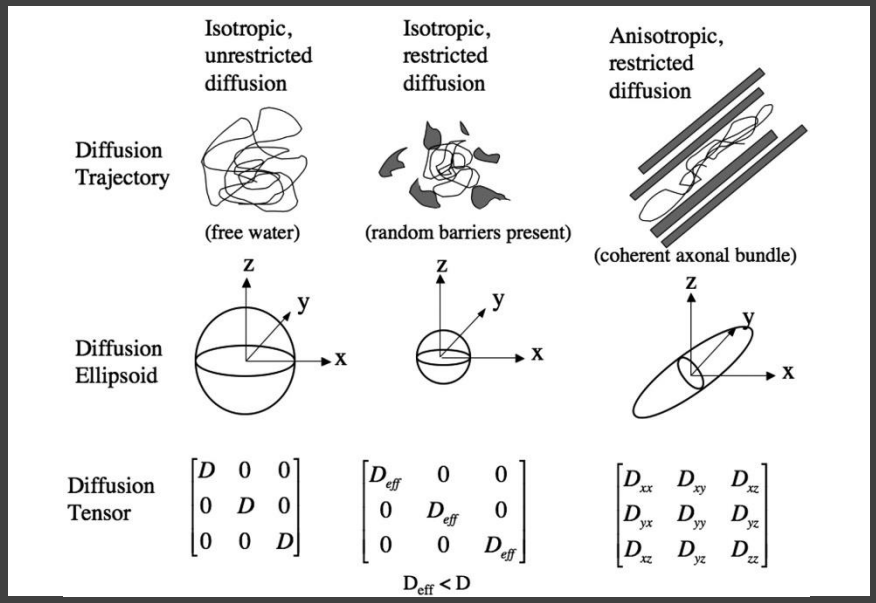
Had been evaluated in stroke in WBIC, Cambridge

Prof Gillard : Any role in imaging of brain tumours?





Price SJ, Burnet NG, Donovan T, Green HA, Peña A, Antoun NM, Pickard JD, Carpenter TA, Gillard JH. Diffusion tensor imaging of brain tumours at 3T: a potential tool for assessing white matter tract invasion?Clin Radiol. 2003 Jun;58(6):455-62.



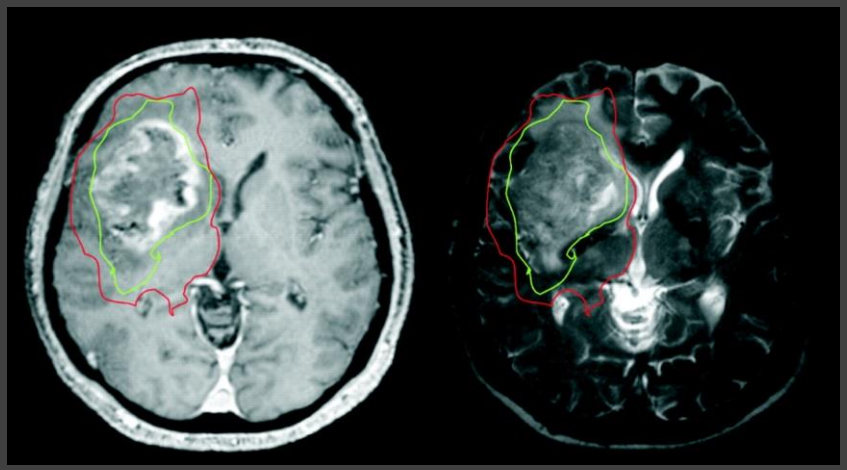
Water diffusion tensor = 6 unique scalars per voxel

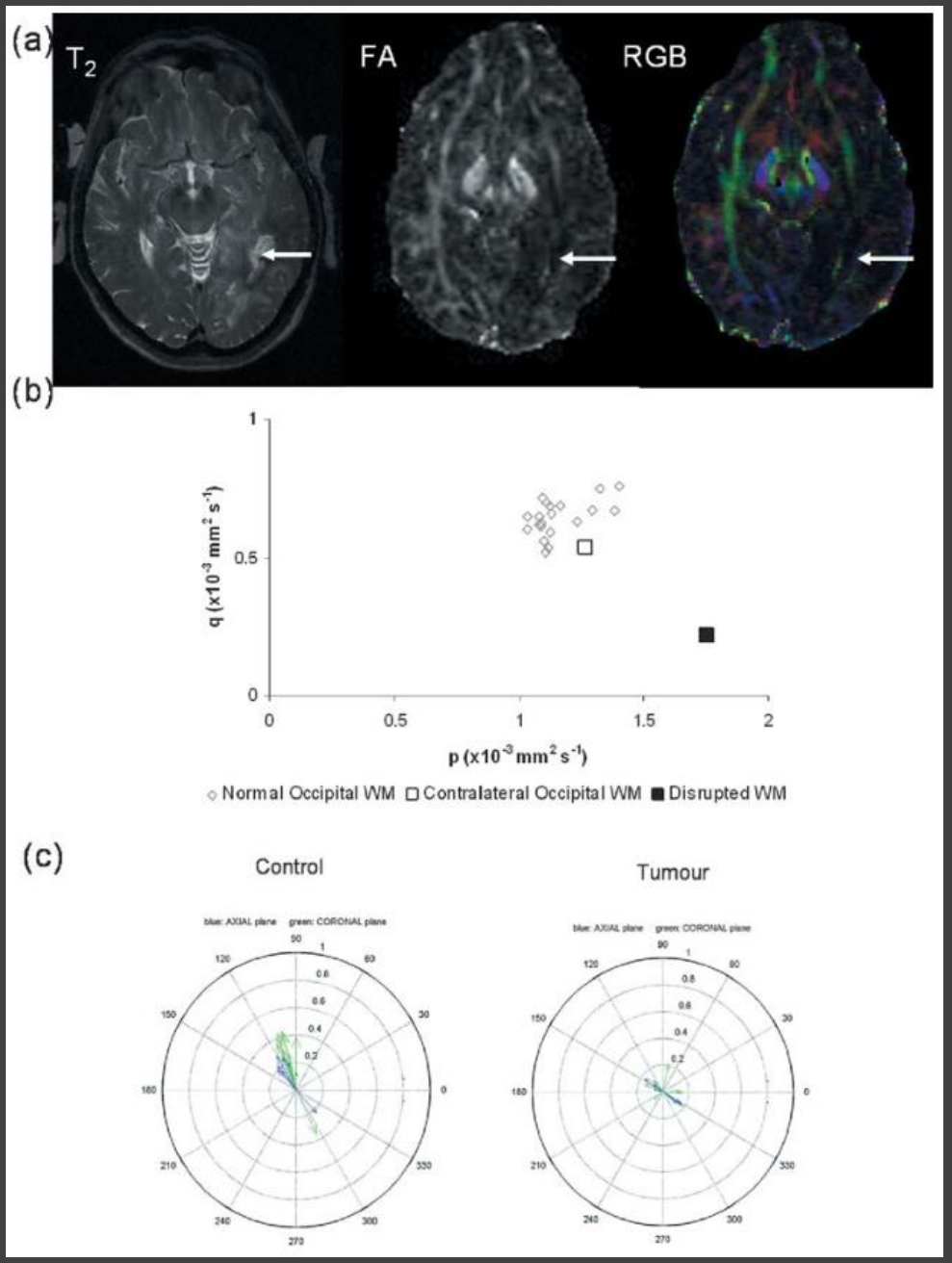
Not all patients showed such ‘barn door’ changes

Need to reduce data to a scalar image map

Alonso Pena applied PCA type approach

Tumour infiltration zone has characteristic ‘tissue signature’

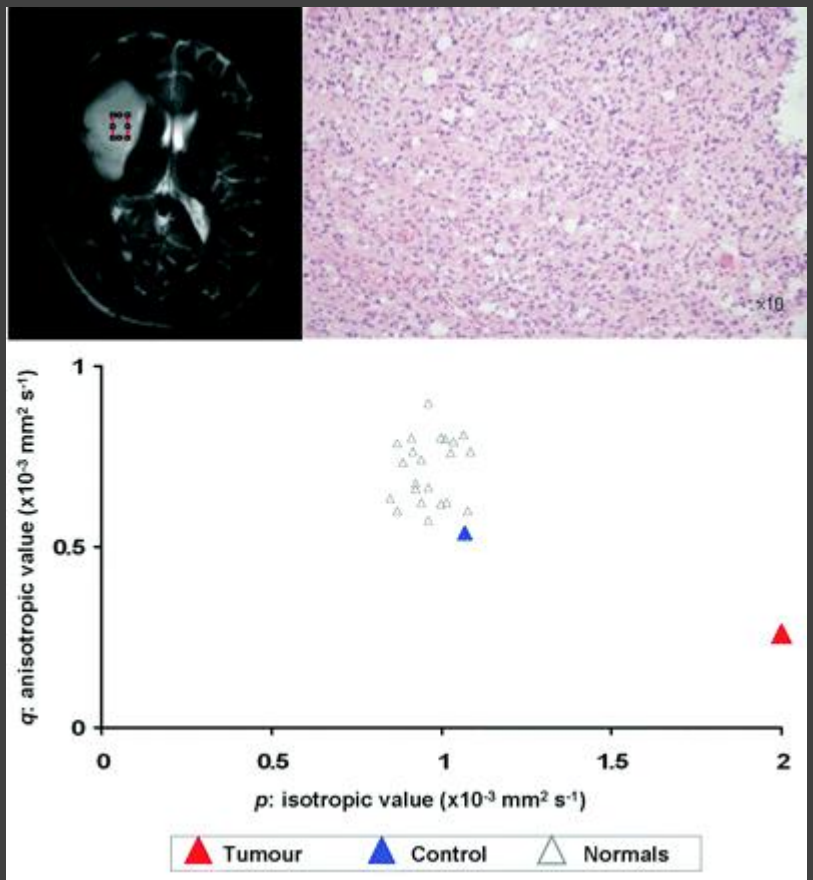




DTI Biopsy study : Stephen Price

Visualise tumour infiltration that appears normal on T2-weighted images in 40% of cases

Sensitivity of 98% and specificity of 81%.



Price SJ, Jena R, Burnet NG, Hutchinson PJ, Dean AF, Peña A, Pickard JD, Carpenter TA, Gillard JH. Improved delineation of glioma margins and regions of infiltration with the use of diffusion tensor imaging: an image-guided biopsy study. AJNR Am J Neuroradiol. 2006 Oct;27(9):1969-74.

Use DTI as basis of individualised tumour volumes

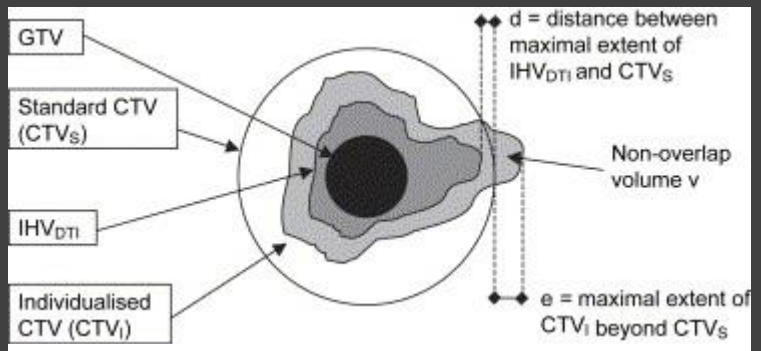
Painstaking manual analysis of DTI FA maps

Most of a week to analyse 1 patient!

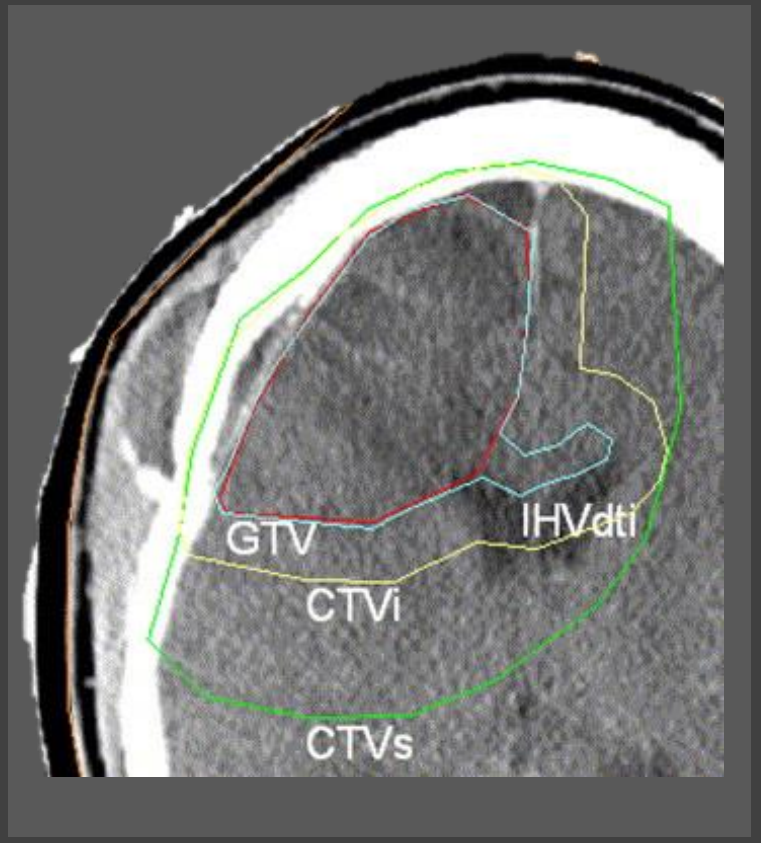
But

Technique had potential to make significant reduction in the size of irradiated volume

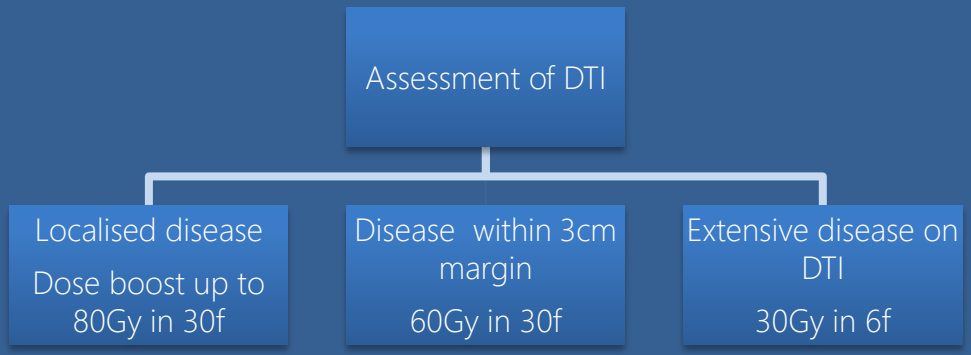
Allow for modest RT dose escalation



Jena R, Price SJ, Baker C, Jefferies SJ, Pickard JD, Gillard JH, Burnet NG. Diffusion tensor imaging: possible implications for radiotherapy treatment planning of patients with high-grade glioma. Clin Oncol (R Coll Radiol). 2005 Dec;17(8):581-90.



DTI| GIRO STUDY (2007-11)

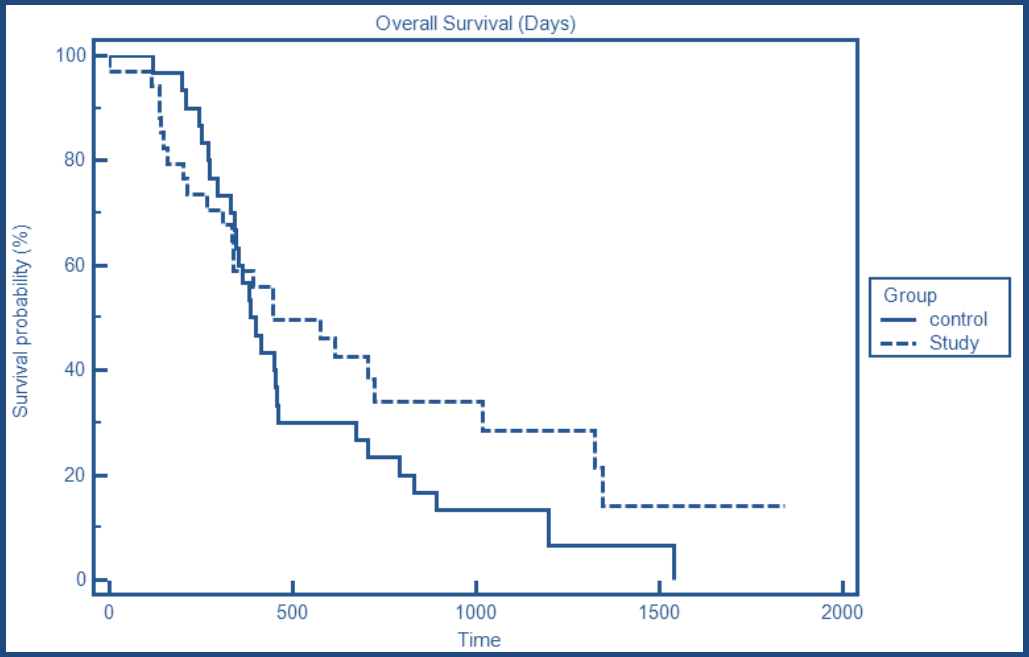


Prospective clinical trial of DTI based radiotherapy individualisation and dose boost

Intensity modulated radiotherapy used to deliver boost dose

60 patients recruited

Improved survival in DTI based RT cohort treated radically

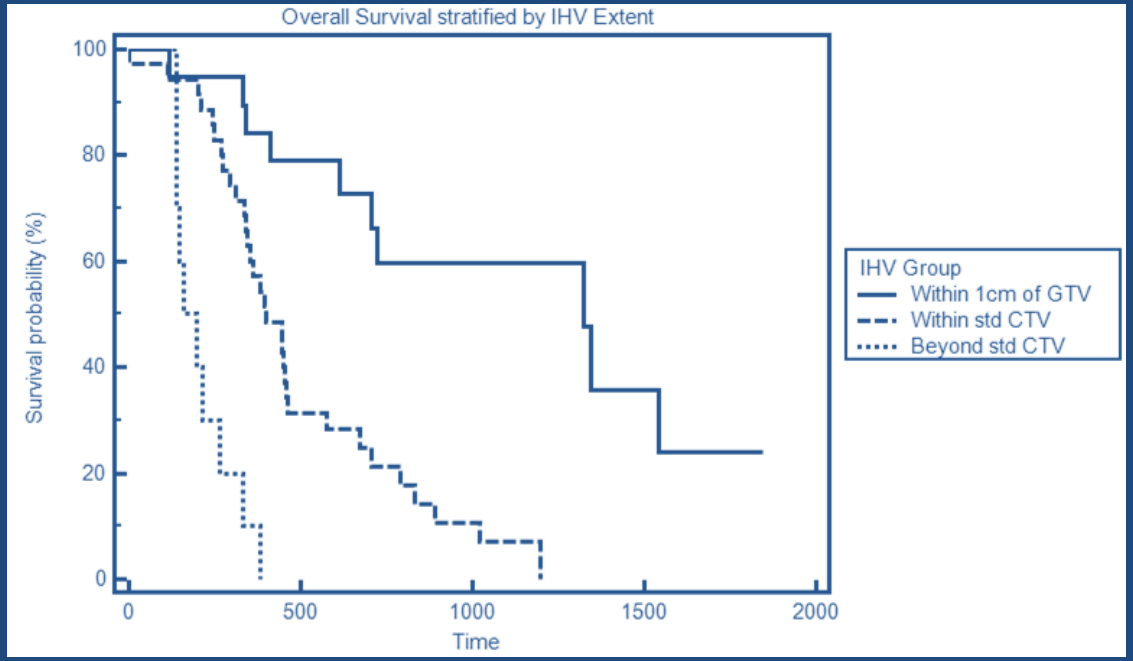


DTI| GIRO SURVIVAL STRATIFICATION

Modest dose boost levels did not impact on patient survival

BUT

Extent of DTI abnormality is highly prognostic of patient survival



GIRO| DTI IMAGE PROCESSING WORKFLOW

By start of GIRO study (2007)

GE 1.5T magnets with turnkey DTI sequences DTI data stored to PACS in DICOM format.

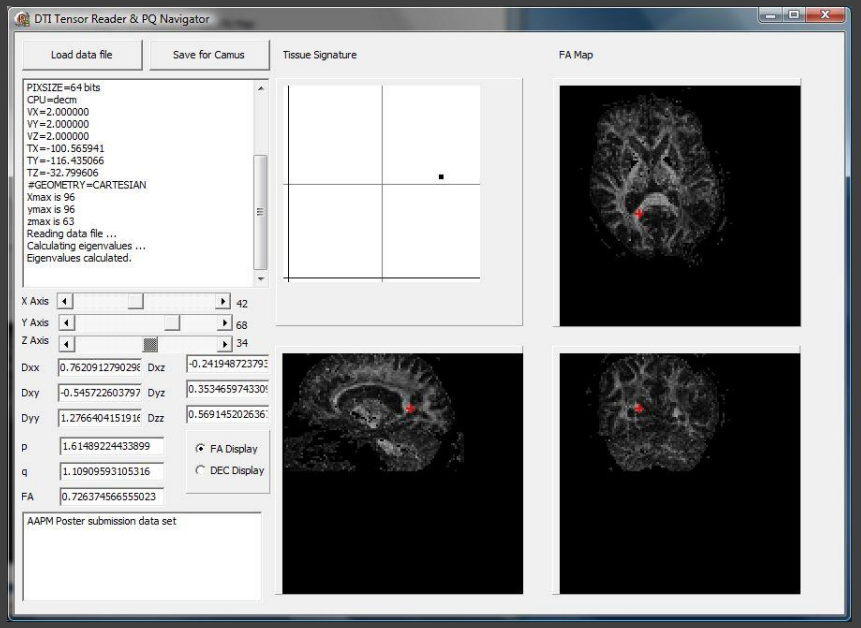
FA maps calculated on scanner

Mature software applications for tensor reconstruction (FSL, Medinria)

Able to write my own software for tensor decomposition maps

Image preparation time around 1 hour per patient

Time to start doing something interesting with the image data …



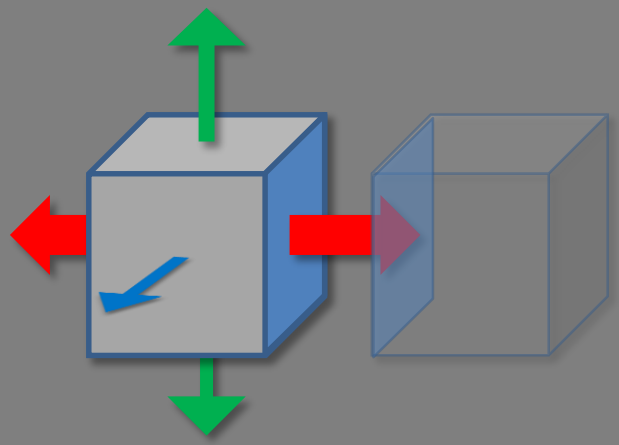
"If in doubt, build a model!"

Swanson & Murray – used reaction-diffusion model to simulate 3D growth patterns of glioma

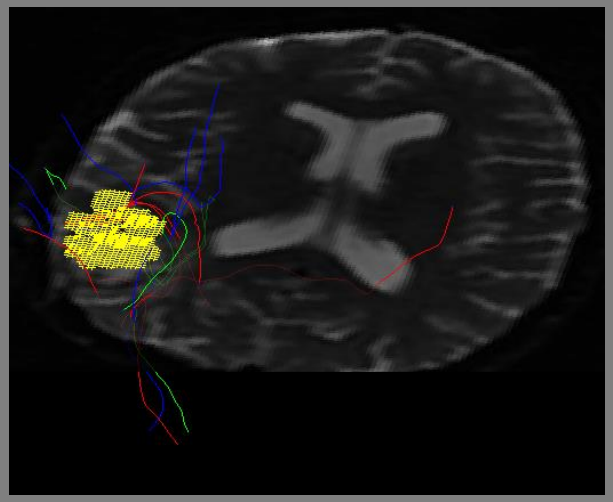
DTI data could be used to build an anisotropic growth model

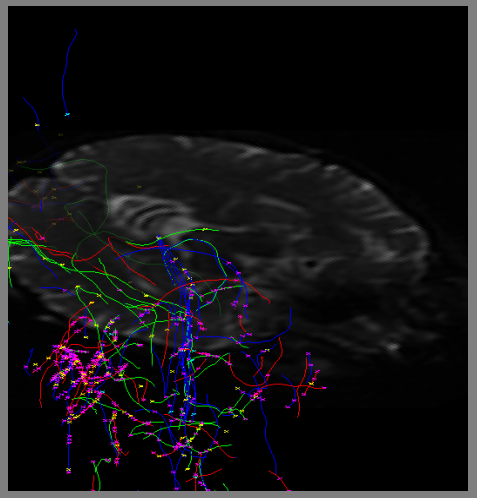
Standard with Cellular Automaton models based on 3D Voxel grid

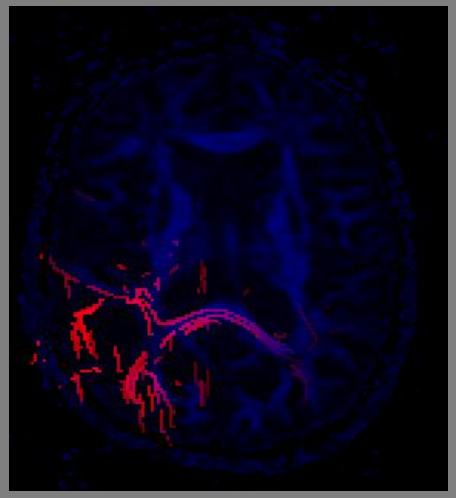
CAMUS : Moved to a Monte-Carlo simulation of tumour migration to construct probabilistic maps of tumour spread for RT Planning



$$Flux = -D_{eff\_w} \cdot D_{eff\_t} \cdot (c_2 - c_1)$$





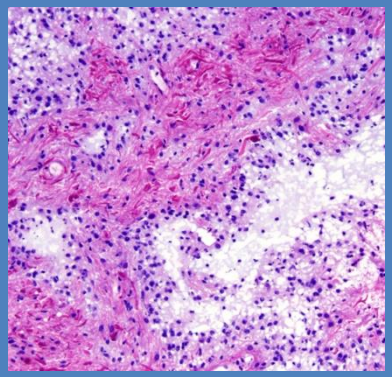


SEGUE

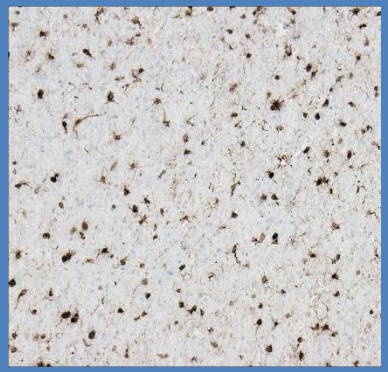
"If I had asked people what they wanted, they would have said faster horses."

Henry Ford

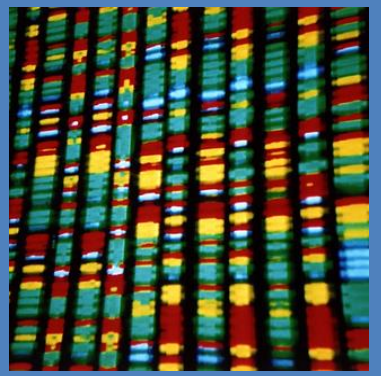
Correlate image based model with tumour biology …



Microscopy



Immunohistochemistry



Molecular Pathology

… for lots and lots of patients, in near real time

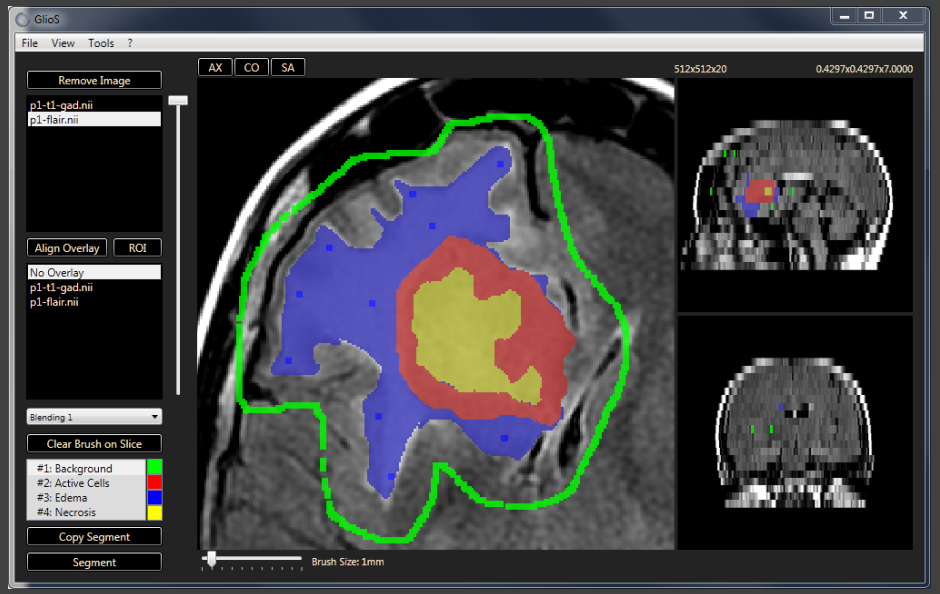
A Big Data problem

Taking baby steps with MSR…

Glios / Autoglios | Criminisi

Fast interactive 3D segmentation based on geodesic distances. RT-ready tumour segmentations in under a minute.

Decision forest ML algorithm for fully automatic segmentations

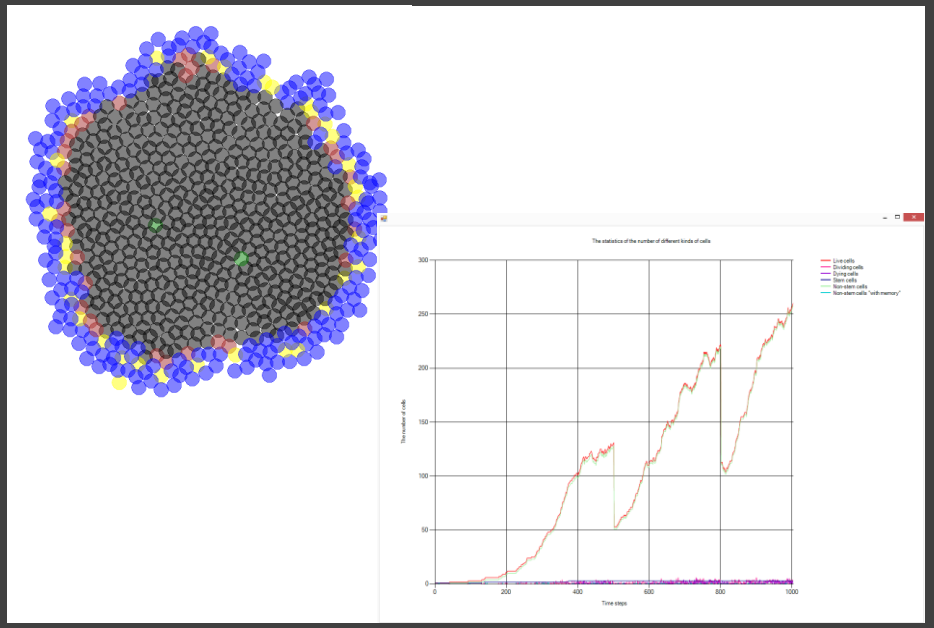


Ayatana | Fisher

Leverage expertise from executable biology models, using power of F#

Encode understanding of tumour micro-environment

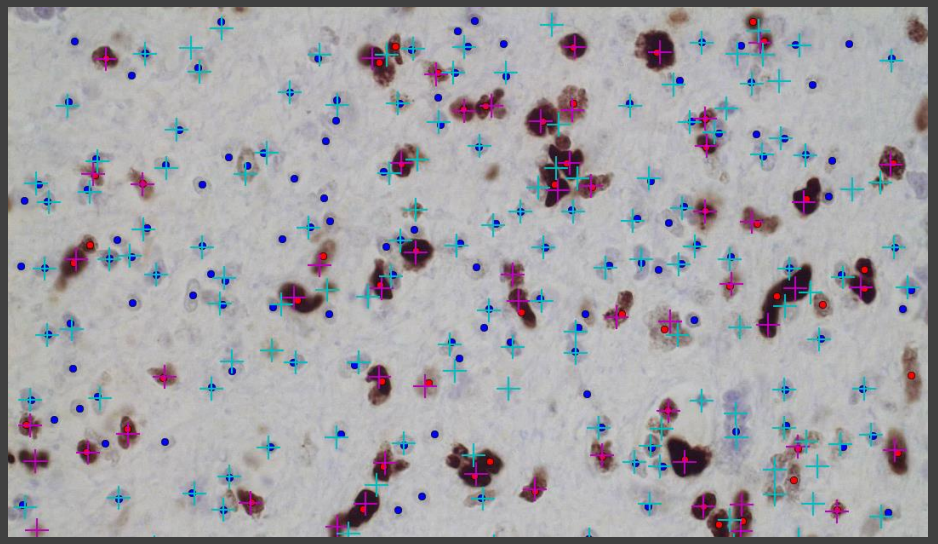
Built a virtual in-vitro glioma, capable of simulating response to radiation



MIB Project | Zikic

Rapidly developed SVM algorithm for quantification of tumour proliferation rates from pathology slides

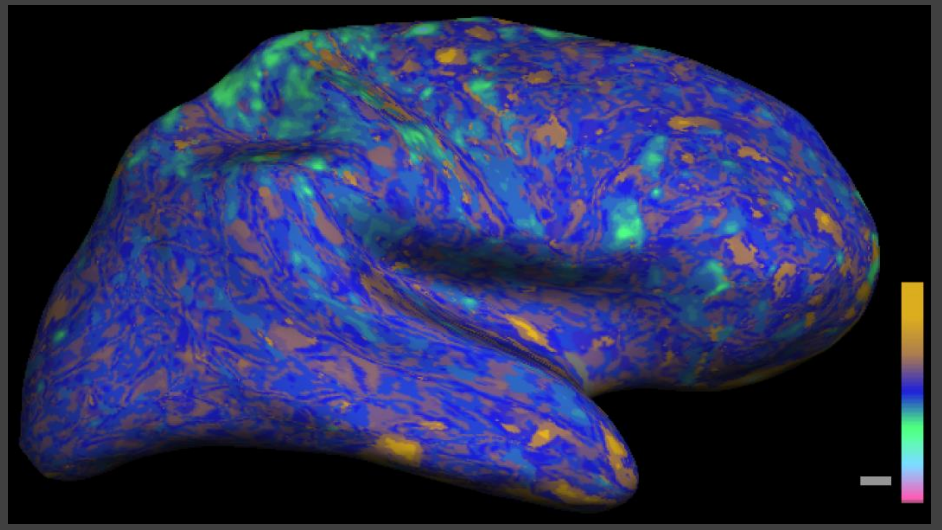
Stunning workflow acceleration!



DTI++| Alexander

NODDI – tissue microstructure model for diffusion MRI

Separate the treatment effect from structural changes in the brain caused by tumour



CONCLUSION

We embrace image processing in so many aspects of our day to day life. It is a disruptive technology placing demands on information governance…

… and we should **keep on pushing** to do the same for image processing in cancer care. After own, it's only lives at stake!

THANKS

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Nicolas Toussaint

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