Biomarkers from Dynamic Images – Approaches and Challenges

Mike Hayball

Cambridge Computed Imaging Ltd (A Feedback PLC Company)

Big Data, Multimodality & Dynamic Models in Biomedical Imaging
Wednesday 9th March 2016, Isaac Newton Institute, Cambridge

CADRAN

TEXRAD

Quantitative Imaging

Quantitative imaging is the extraction of quantifiable features from medical images for the assessment of normal or the severity, degree of change, or status of a disease, injury, or chronic condition relative to normal.

(Quantitative Imaging Biomarkers Alliance – QIBA)

Imaging biomarkers

A quantitative imaging biomarker (QIB) is an objective characteristic derived from an in vivo image MEASURED on a ratio or interval scale as indicators of normal biological processes, pathogenic processes or a response to a therapeutic intervention.

(Quantitative Imaging Biomarkers Alliance – QIBA)

Quantitative Dynamic imaging

- Quantitative imaging biomarkers from time series of images:
  - Nuclear Medicine
  - Positron Emission Tomography (PET)
  - Transmission X-ray - Iodinated contrast
  - X-ray Computed Tomography - Iodinated contrast
  - Ultrasound
  - Magnetic Resonance Imaging
    - Injected contrast
    - Arterial Spin Labelling
    - Diffusion Weighted Imaging

"Colour Perfusion" Imaging 1991

Colour perfusion imaging: a new application of computed tomography

K. A. MILES M. HAYBALL A. K. DIXON

We describe a new application for imaging with computed tomography (CT) in which a quantifiable map of tissue perfusion is created and displayed by means of a colour scale. A rapid sequence of images is acquired without table movement immediately after a bolus intravenous injection of radiographic contrast medium. The rate of enhancement in each pixel within the chosen slice can then be used to determine perfusion. The technique provides a quantifiable display of regional perfusion combined with the high spatial resolution afforded by CT.

Lancet 1991; **337**: 643–45

Tissue perfusion can be measured by means of dynamic computed tomography (CT) by adaptation of a nuclear medicine data-processing technique.[1,2] A rapid sequence of

Present

B-0435 11:10
Texture analysis of blood flow maps in CT perfusion studies of NSCLC: correlation with the overall survival
S. Baiocco[1], D. Barone[2], G. Gavelli[2], A. Bevilacqua[1]; [1]*Bologna/IT*, [2]*Meldola/IT*
(s.baiocco@unibo.it)

B-0434 11:02
Improvement of perfusion characterisation in two lung tumour subtypes using de-noised CT perfusion maps
S. Baiocco[1], D. Barone[2], G. Gavelli[2], A. Bevilacqua[1]; [1]*Bologna/IT*, [2]*Meldola/IT*
(s.baiocco@unibo.it)

History - Axel

Cerebral Blood Flow Determination by Rapid-Sequence Computed Tomography

A Theoretical Analysis[1]

Leon Axel, M.D., Ph.D.

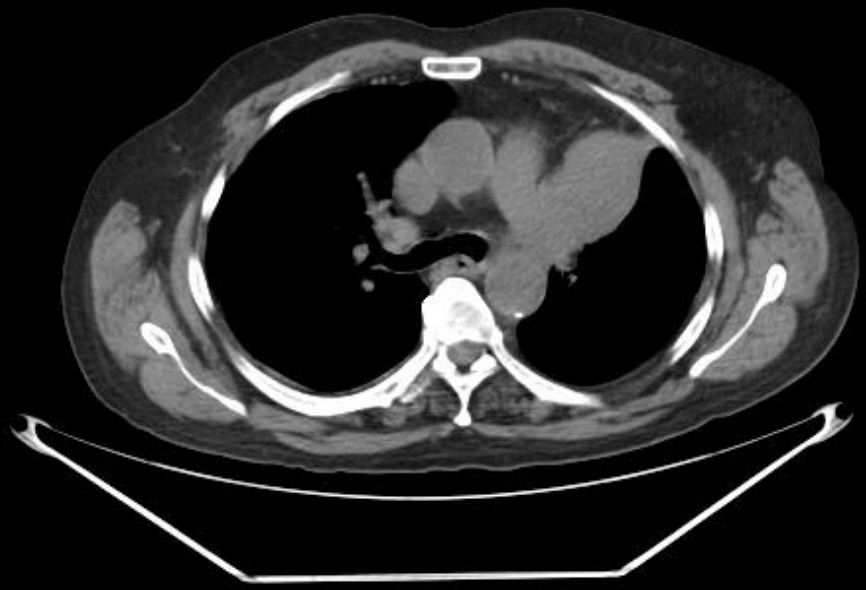
Dynamic computed tomography (CT) using rapid-sequence scanning can be used to determine cerebral blood flow noninvasively following an intravenous bolus injection of contrast material. Since the contrast material remains intravascular in the normal brain, principles of indicator dilution analysis for nondiffusible indicators are applied to the time course of the changes in contrast concentration. While a delay is introduced by the relatively prolonged intravenous injection, this can be corrected for if the arteries are seen on the scan; the corrected mean transit time of the first passage of the bolus through the vessels gives the blood flow per unit vascular volume. To find the blood flow per unit of total tissue volume requires measuring the concentration of contrast material in the blood, which cannot always be done directly from brain scans with current CT equipment; however, a relative value for total tissue flow can be found by using the area under the curve of contrast concentration as a function of time, as this area is proportional to the fractional vascular volume of the tissue.

INDEX TERMS: Blood, flow dynamics • Brain, blood supply (Skull and contents, low flow state, 1[0].760) • Computed tomography, contrast enhancement • Head, computed tomography, 1[0].1211

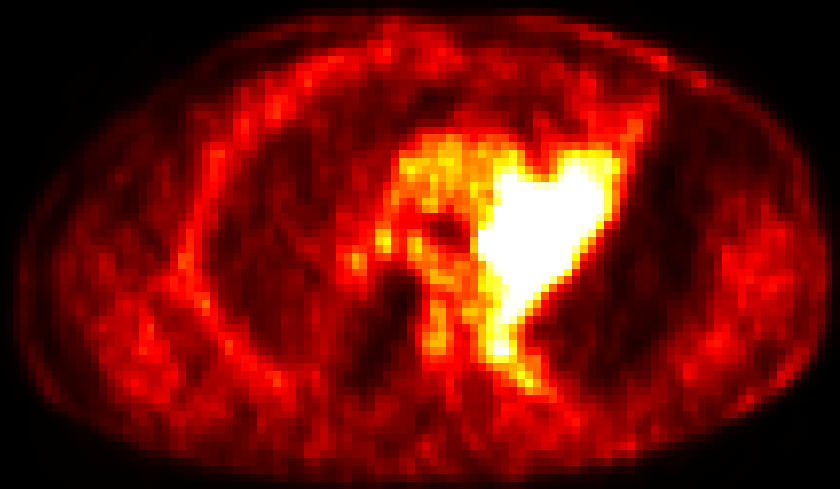
Radiology 137:679–686, December 1980

Anatomy vs Function

Conventional CT
good resolution, poor function

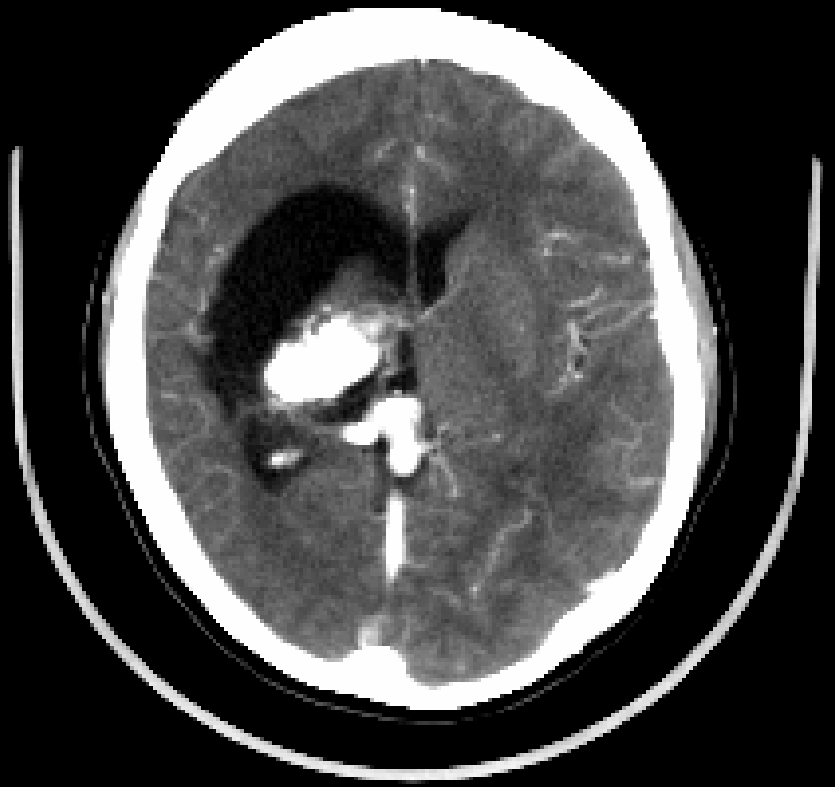


PET/Nuclear Medicine
Good Function, poor resolution

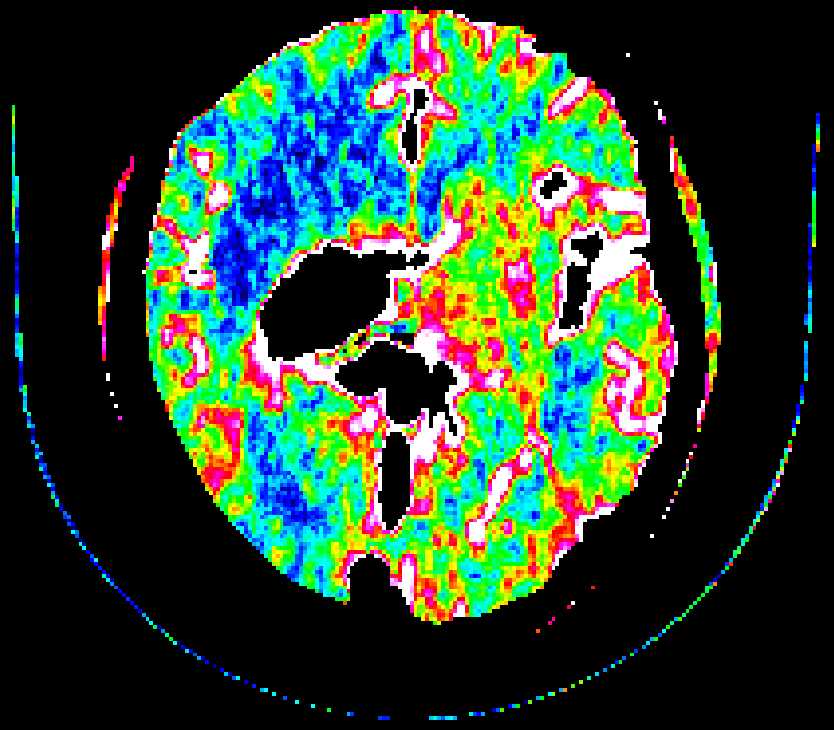


Anatomy and function

Contrast Enhanced CT
good resolution, subjective function



Functional CT
Apply quantitative techniques to single location CT

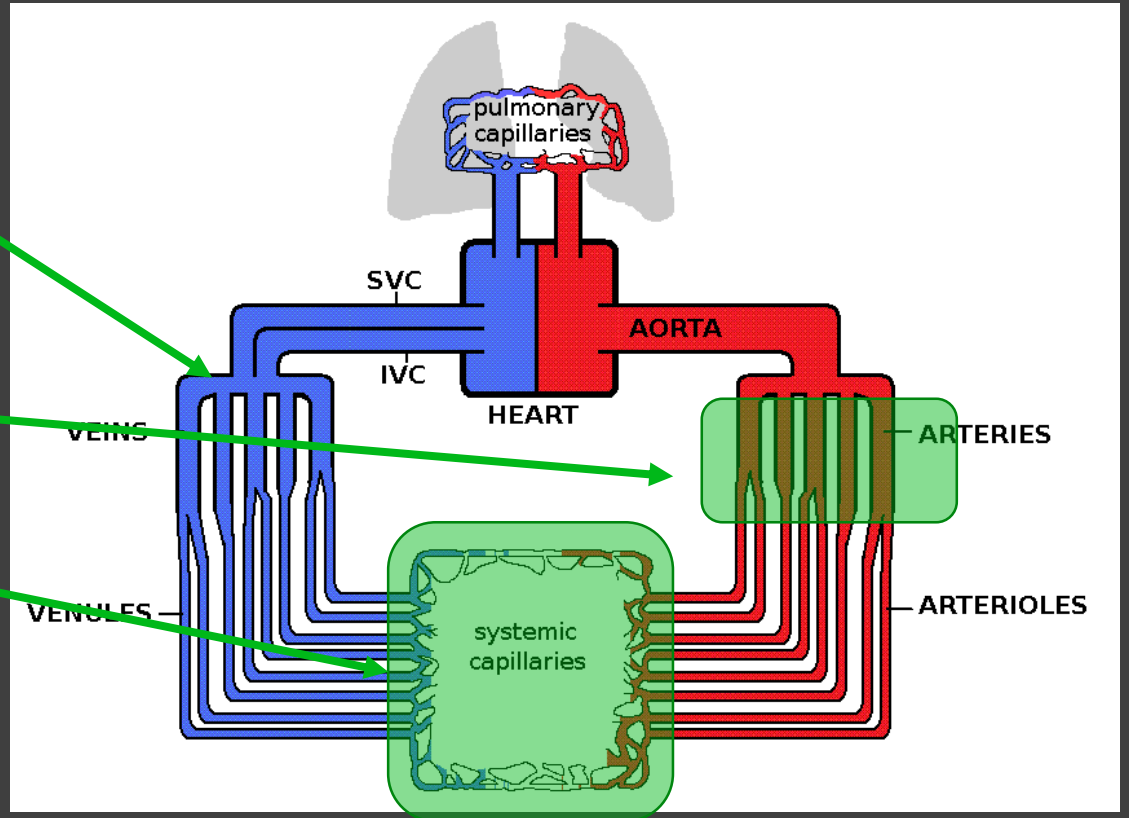


CADRAN

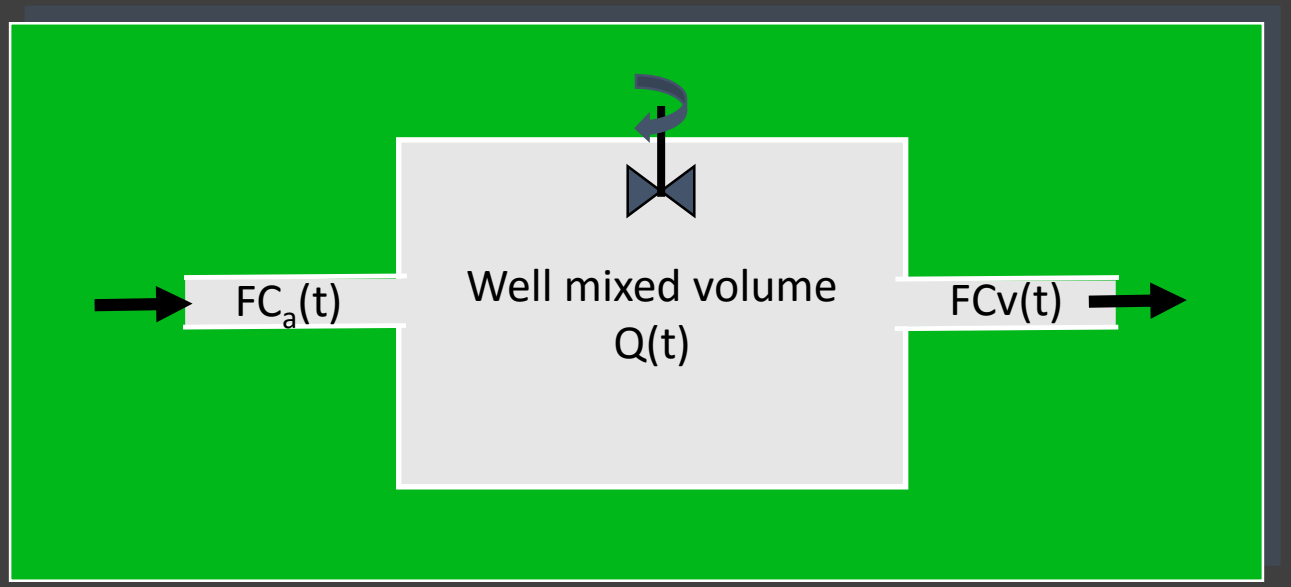
TEXRAD

Perfusion Imaging

- Fast injection of iodinated contrast
- Capture a slice which includes
  - Artery
  - Tissue of interest



Fick Principle (1)



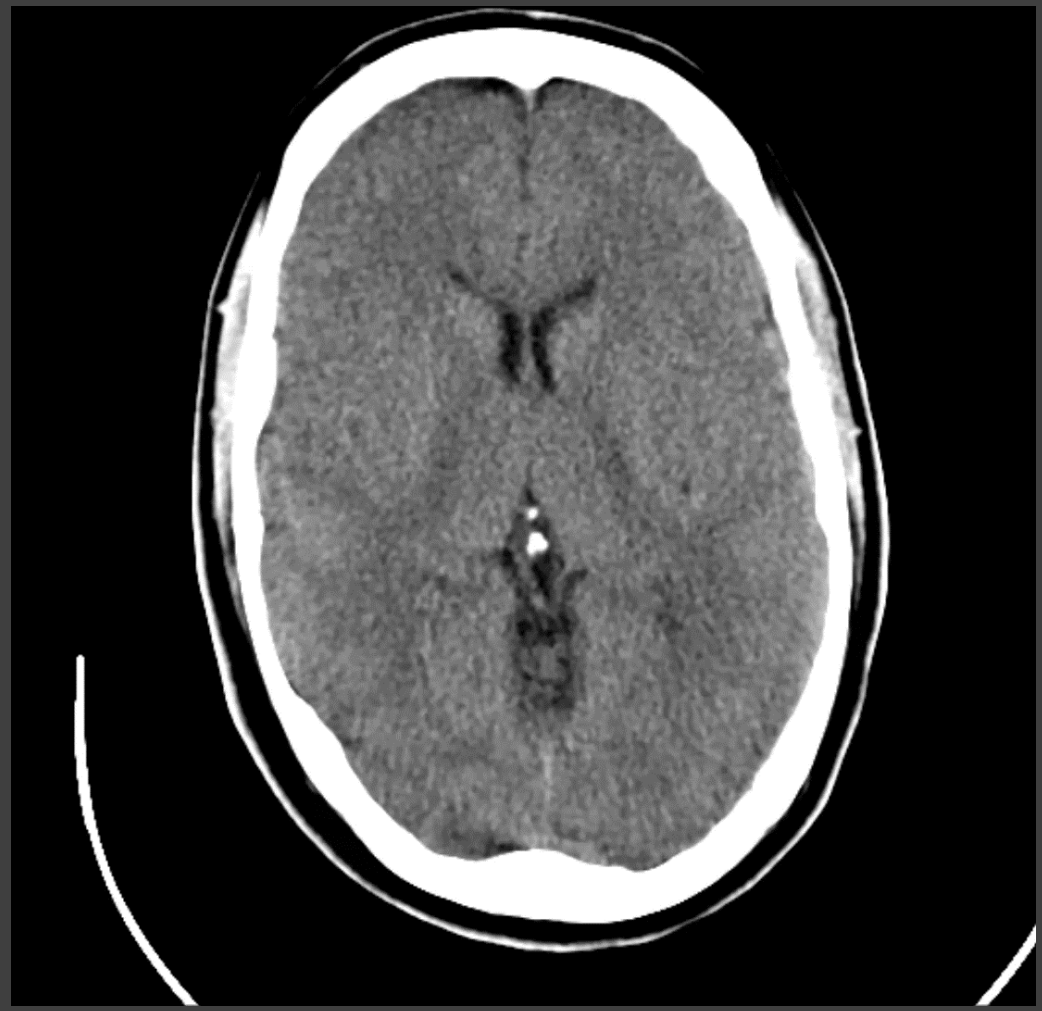
$$Q(t) = F \int_0^t [C_a(t) - C_v(t)]dt$$

CADRAN

TEXRAD

Dynamic sequence

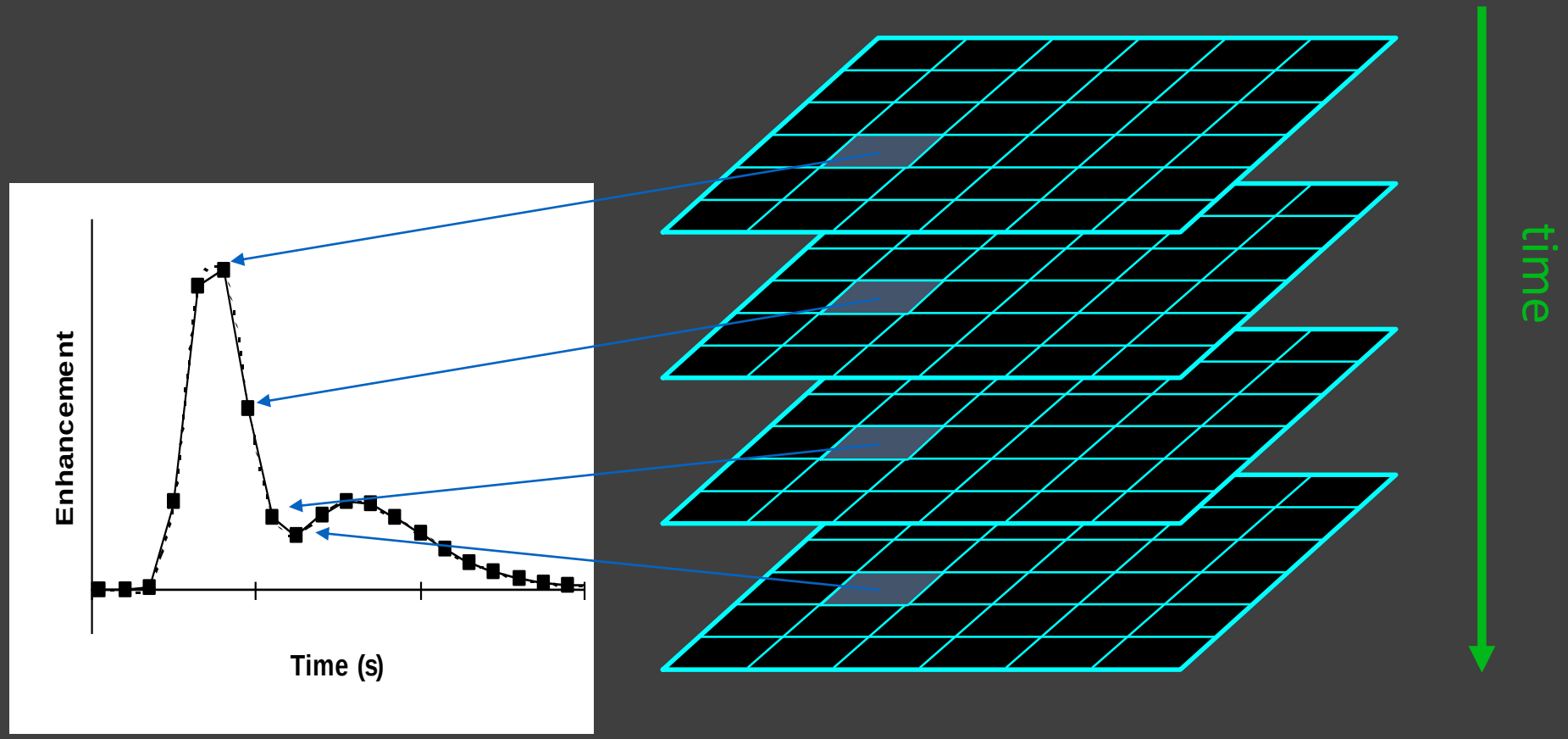
- 10-12 1s images in 45-60 seconds
- Assumptions:
  - CT number proportional to iodine concentration
  - Retention time in tissue > time to peak
  - Contrast pharmaceutically inert



CADRAN

TEXRAD

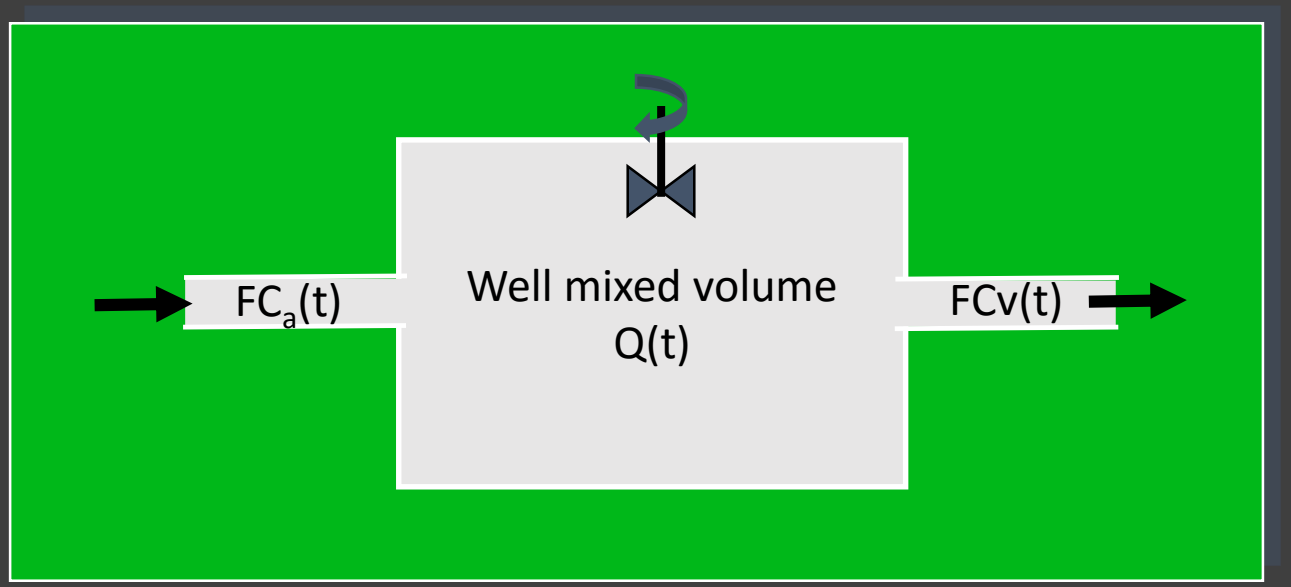
TDC generation



CADRAN

TEXRAD

Fick Principle (1)

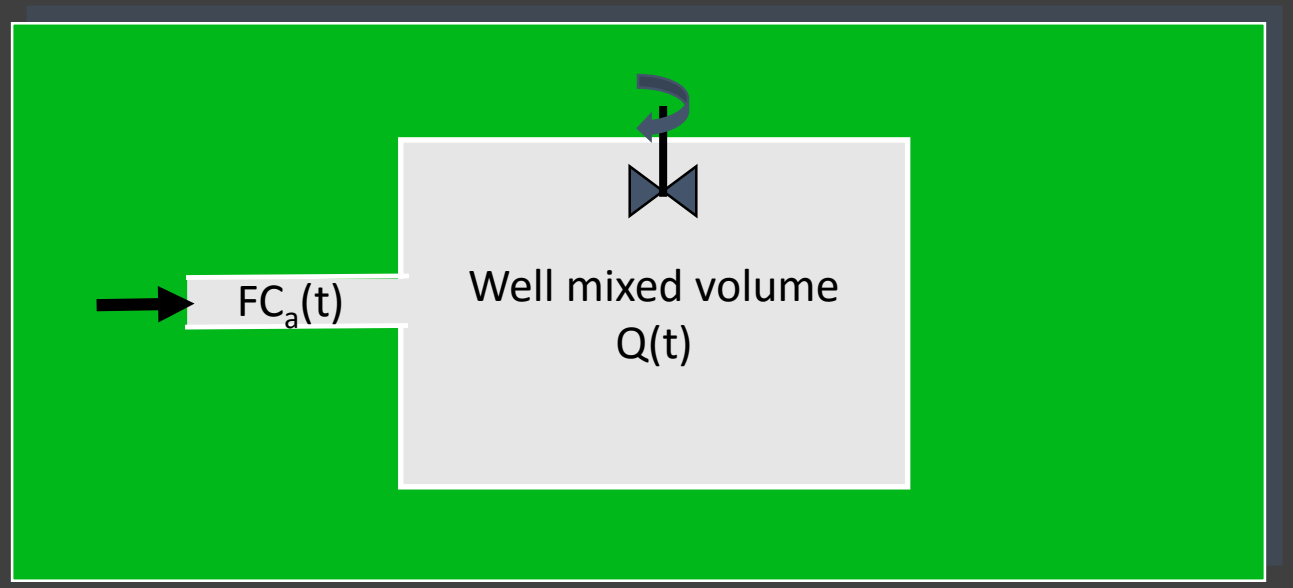


$$Q(t) = F \int_0^t [C_a(t) - C_v(t)]dt$$

CADRAN

TEXRAD

Fick Principle (2)



$$Q(t) = F \int_0^t C_a(t)dt$$

CADRAN

TEXRAD

Fick Principle (3)

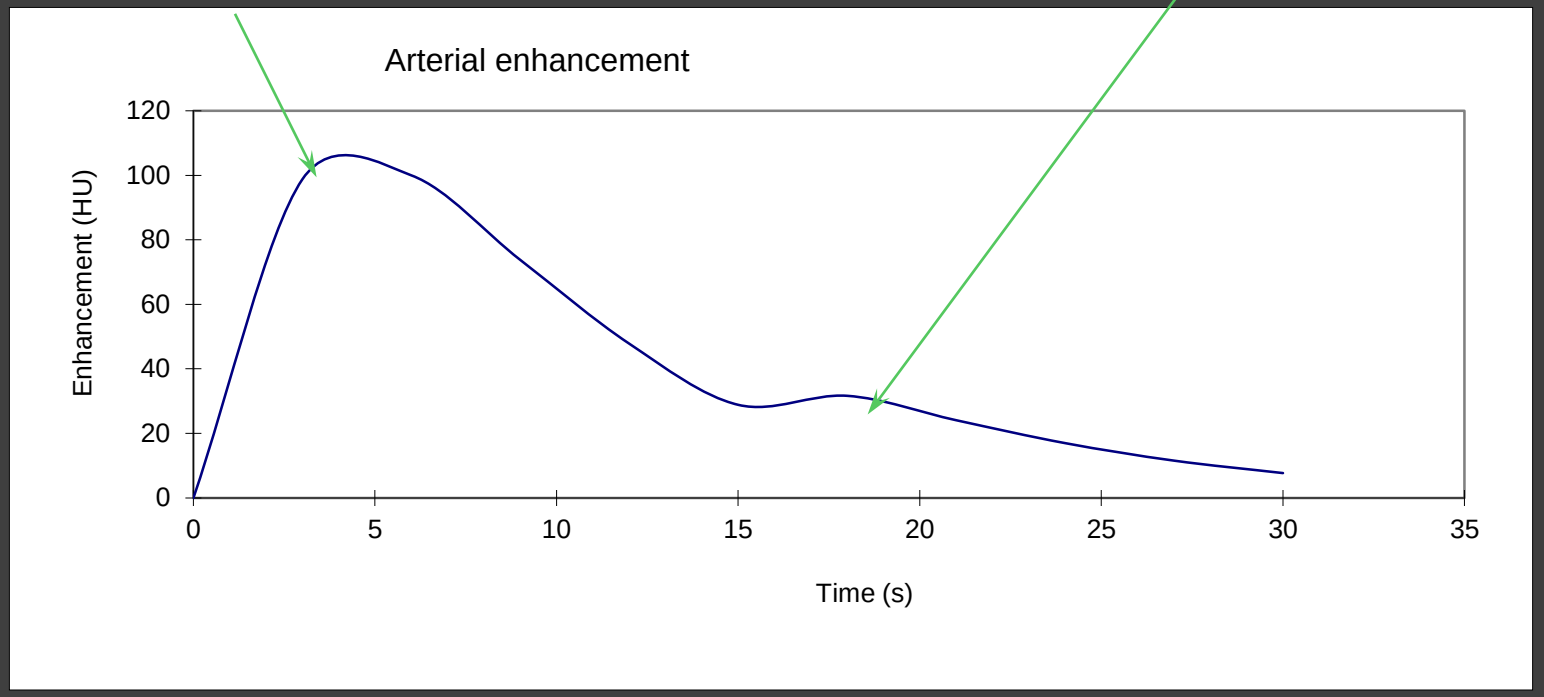
- Assuming no outflow during the inflow phase
  - Requires a fast injection of contrast
- Contrast accumulation is at peak when the arterial concentration reaches maximum

$$Q(t) = F \int_0^t C_a(t)dt \quad \longrightarrow \quad \left[\frac{dQ(t)}{dt}\right]_{max} = F\,[C_a(t)]_{max}$$

Perfusion Imaging

Initial bolus

Recirculation

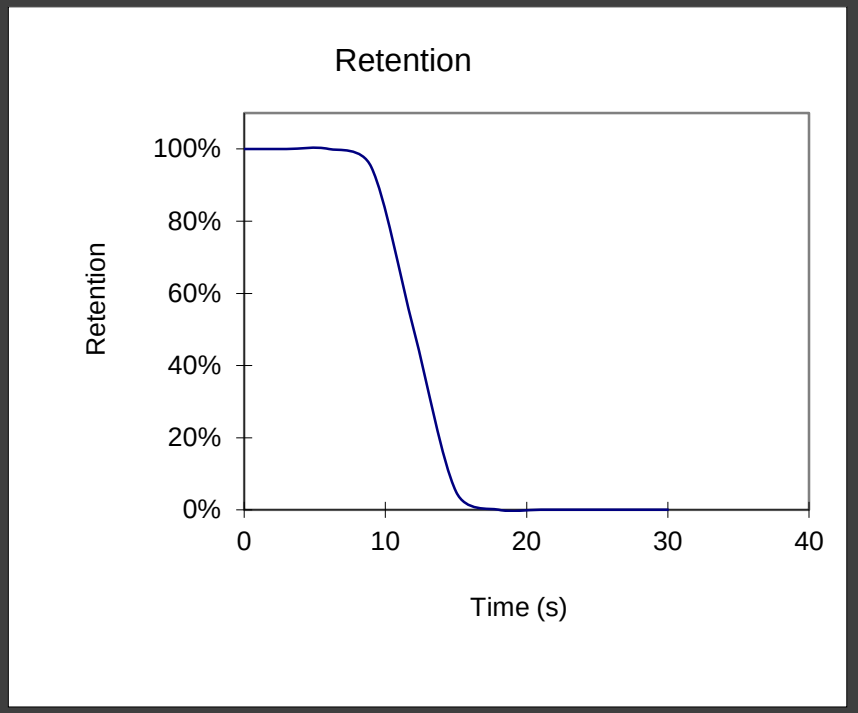


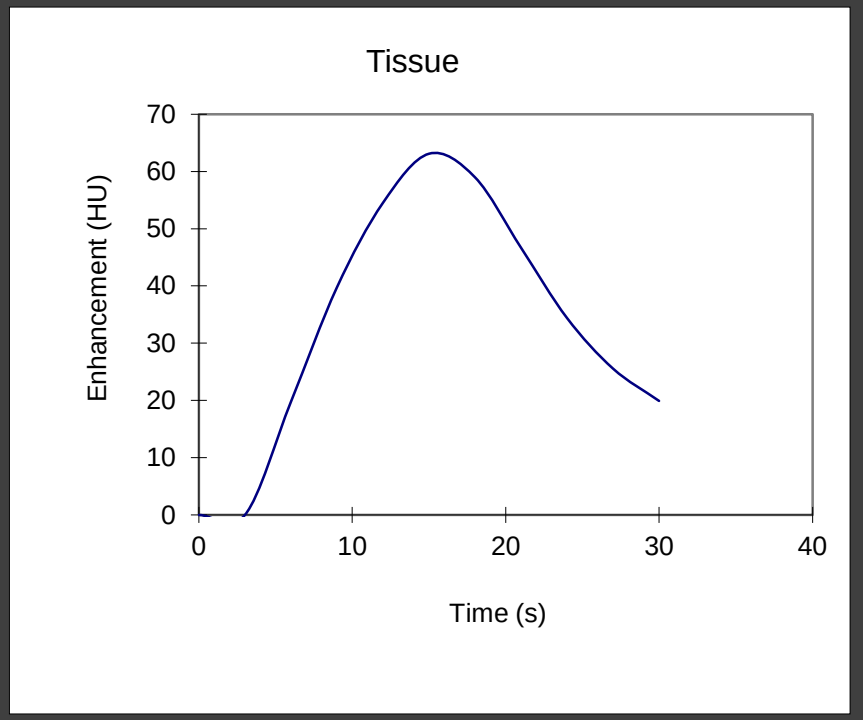
Arterial enhancement following fast bolus injection

CADRAN

TEXRAD

Perfusion Imaging



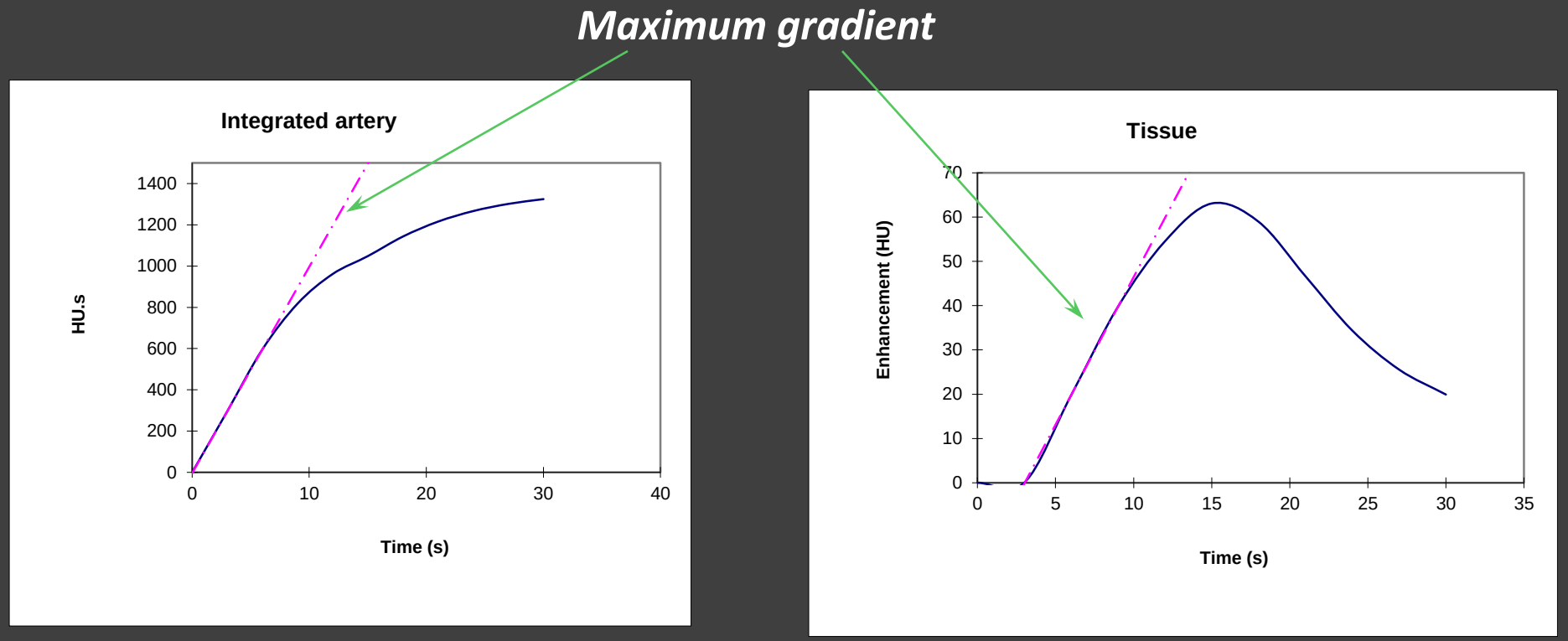


Enhancement in a tissue voxel following bolus injection

CADRAN

TEXRAD

Perfusion



Comparison of integrated arterial TDC and tissue TDC

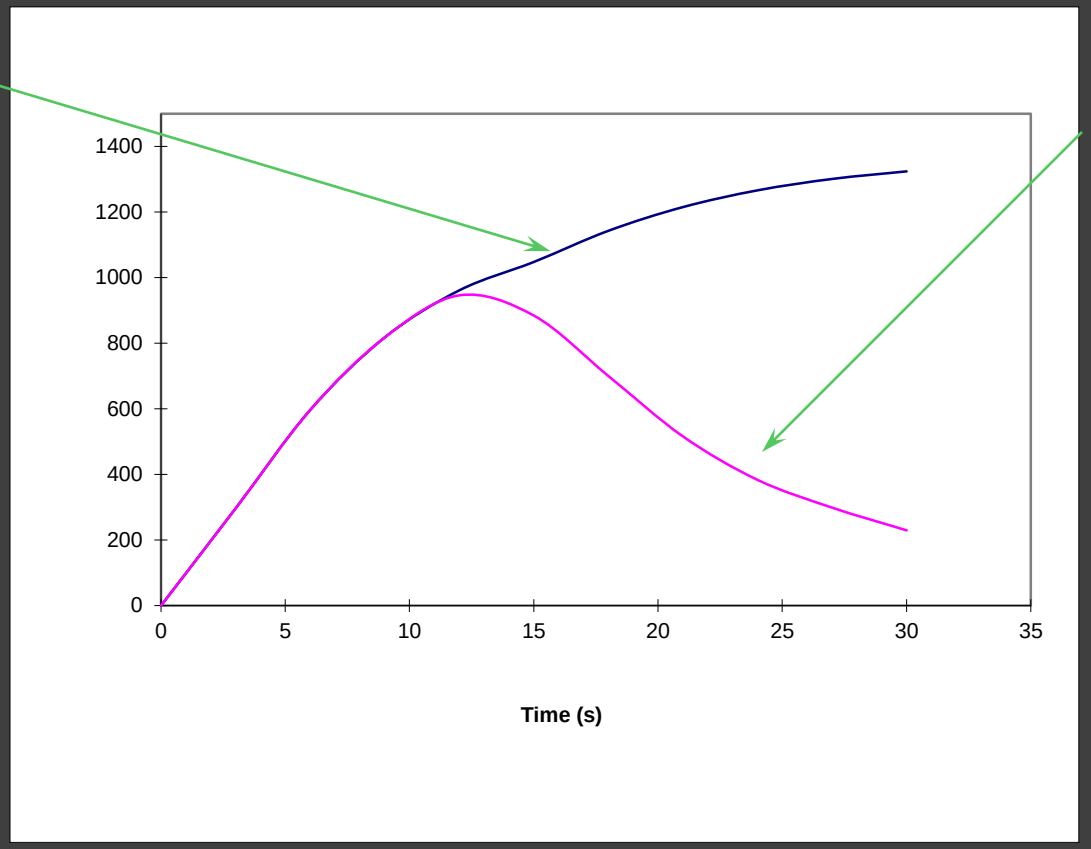
CADRAN

TEXRAD

Perfusion

Integrated artery

Tissue TDC



Integrated artery and tissue TDC matched curves

CADRAN

TEXRAD

Perfusion

$$\text{Perfusion} = \frac{\text{Maximum gradient in tissue}}{\text{Maximum enhancement in artery}}$$

CADRAN

TEXRAD

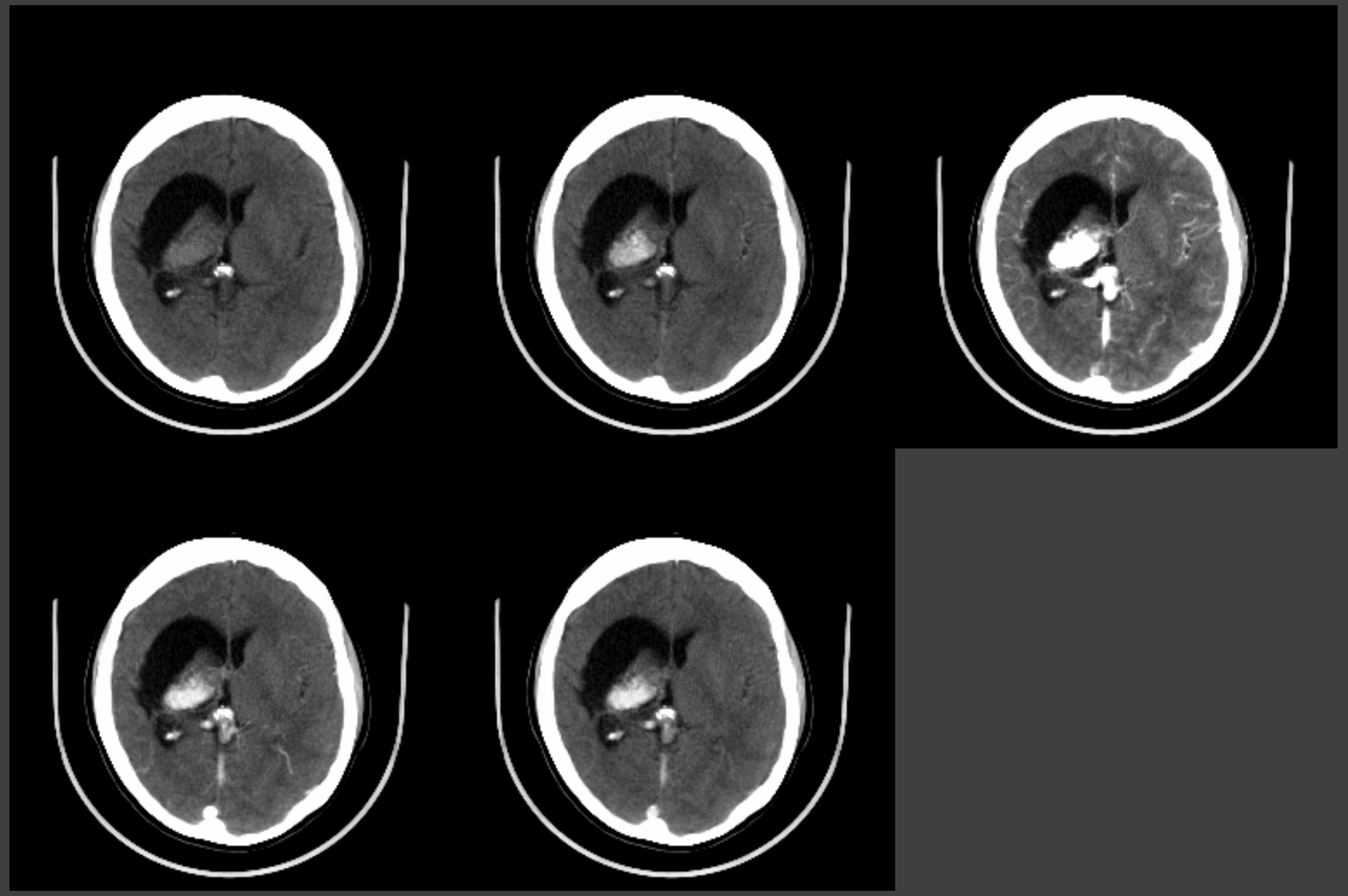
Perfusion

$$\text{Perfusion} = \frac{\text{Maximum gradient in tissue}}{\text{Maximum enhancement in artery}}$$

- A very simple equation…
- We don't need to worry about time delays between artery and tissue curves
- Both values are simple to derive
- Can easily reduce the impact of noise by line fitting etc
- Dividing a small number by a bigger number

CADRAN TEXRAD

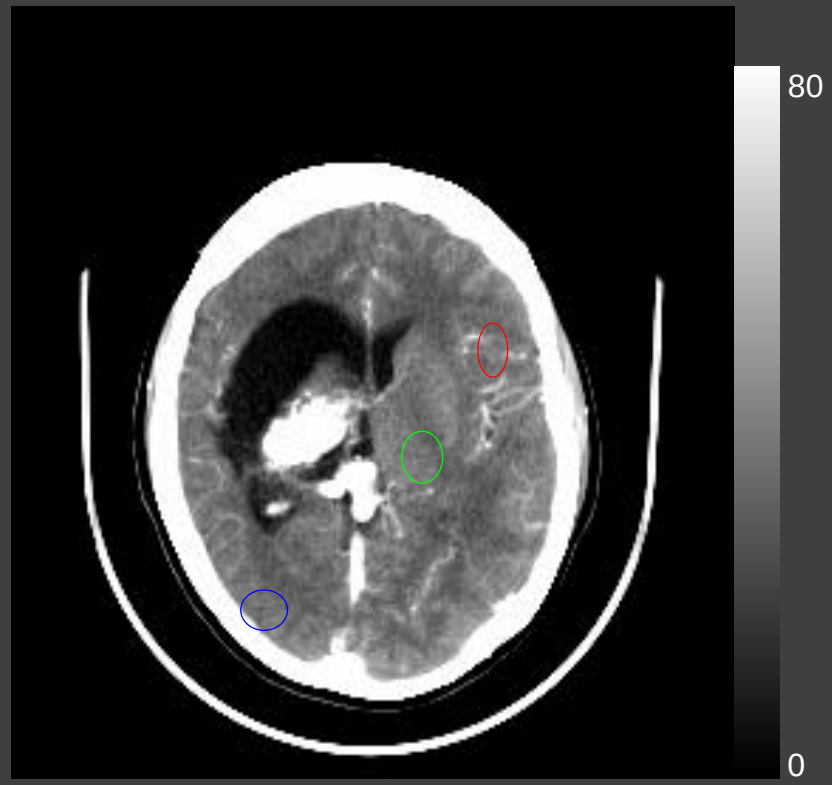
Sample Data

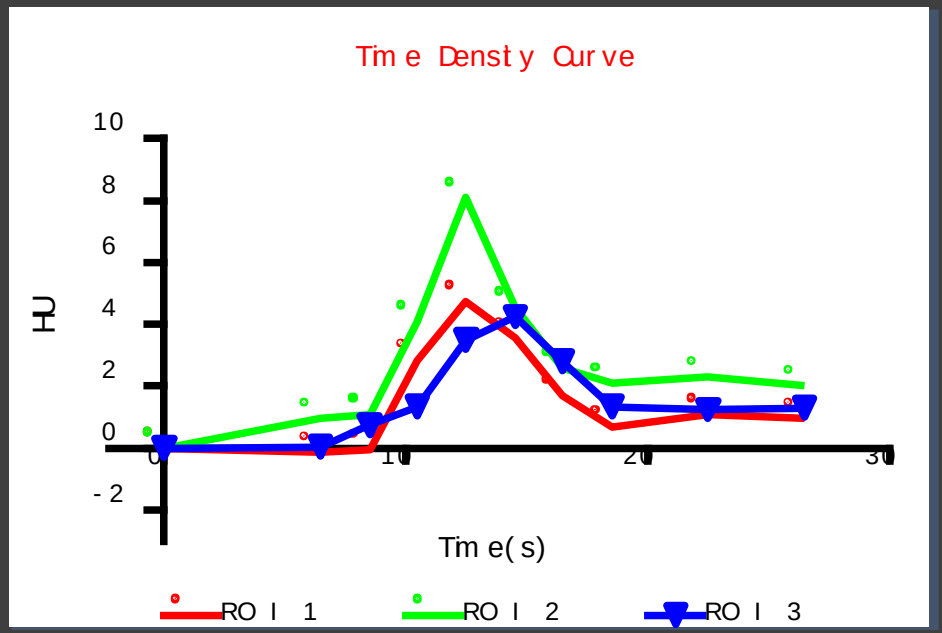


CADRAN

TEXRAD

Region of interest analysis

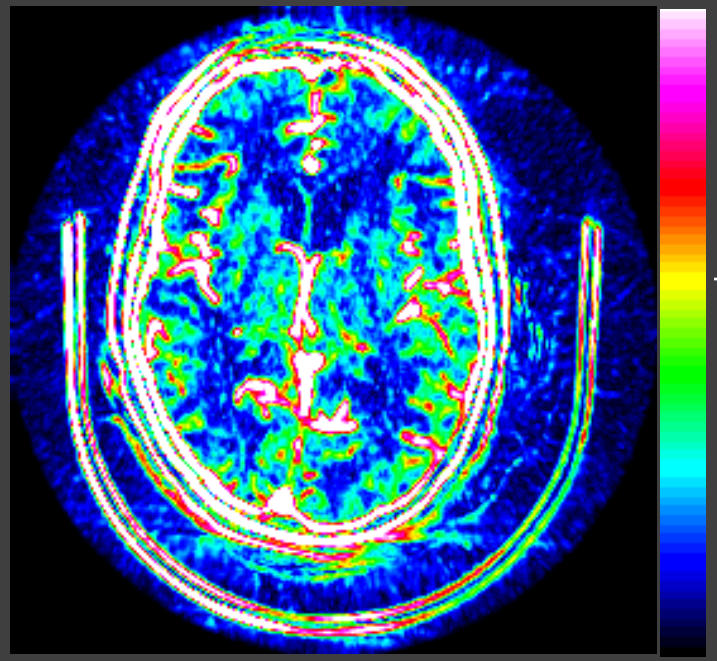




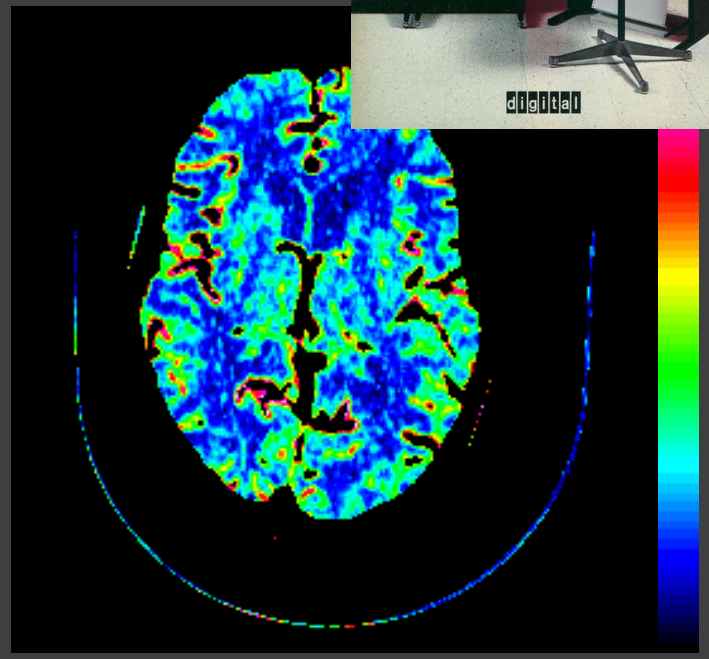
CADRAN

TEXRAD

Thresholding



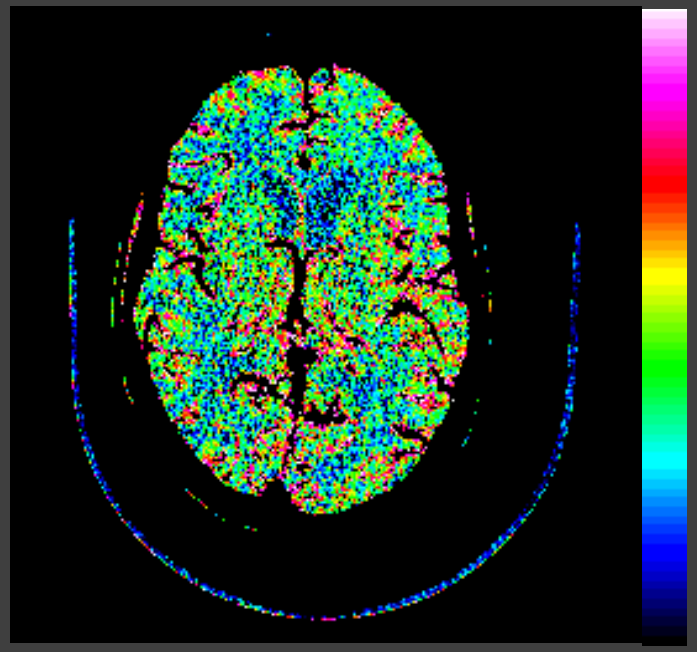
Threshold Applied



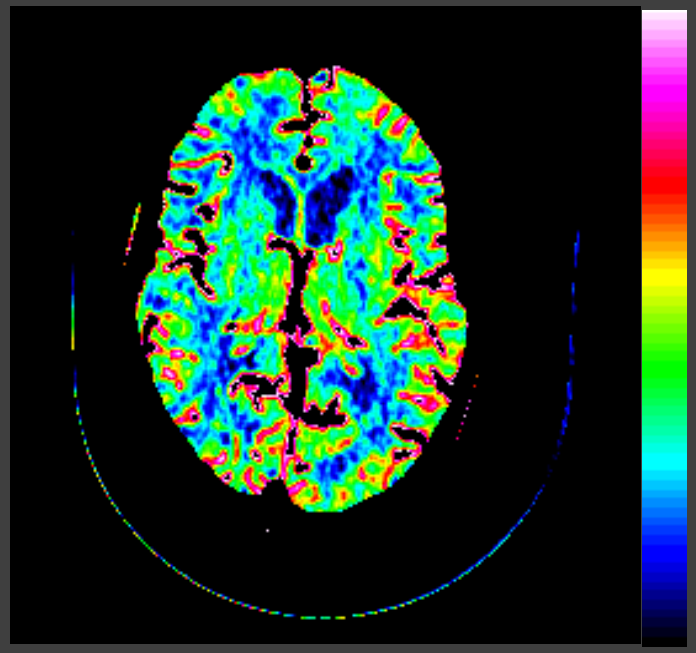
CADRAN

TEXRAD

Smoothing



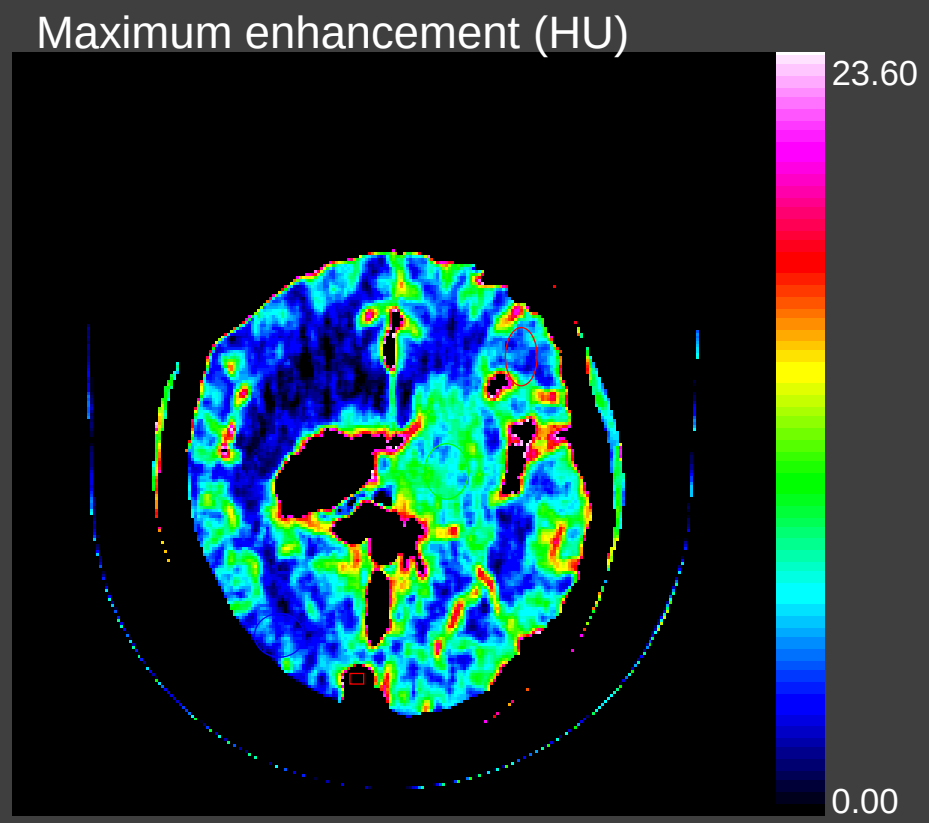
Binomial
smooth



CADRAN

TEXRAD

Maximum enhancement

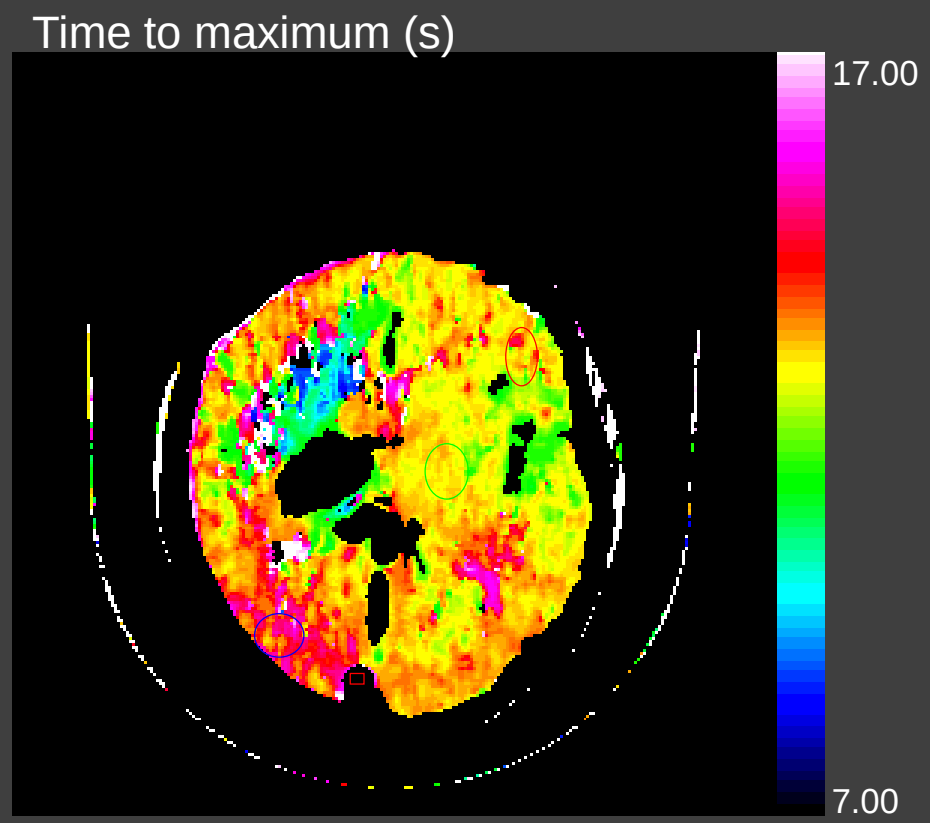


- Measures the peak enhancement for each pixel
- Can be used as an indicator of blood volume

CADRAN

TEXRAD

Time to maximum



- Measures the time of peak enhancement for each pixel
- Indicates time of arrival of the blood supply
- Can be used to diagnose stenosis

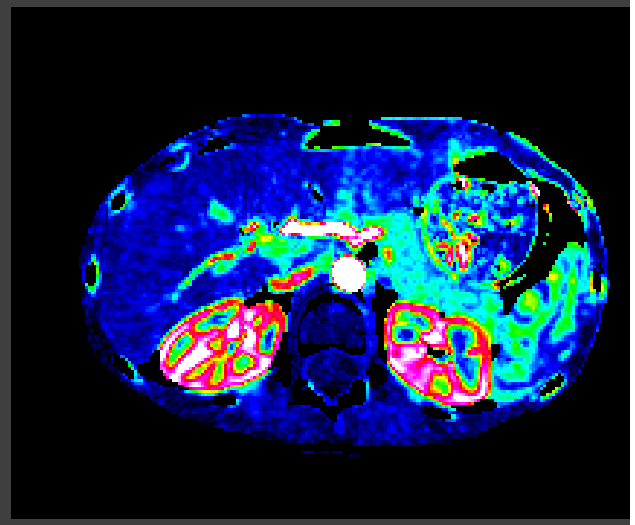
CADRAN

TEXRAD

History – Miles et. al.

Applications:

- Stroke imaging
- Cardiac imaging
- Liver imaging
- Oncology



Colour perfusion imaging: a new application of computed tomography

K. A. MILES M. HAYBALL A. K. DIXON

We describe a new application for imaging with computed tomography (CT) in which a quantifiable map of tissue perfusion is created and displayed by means of a colour scale. A rapid sequence of images is acquired without table movement immediately after a bolus intravenous injection of radiographic contrast medium. The rate of enhancement in each pixel within the chosen slice can then be used to determine perfusion. The technique provides a quantifiable display of regional perfusion combined with the high spatial resolution afforded by CT.

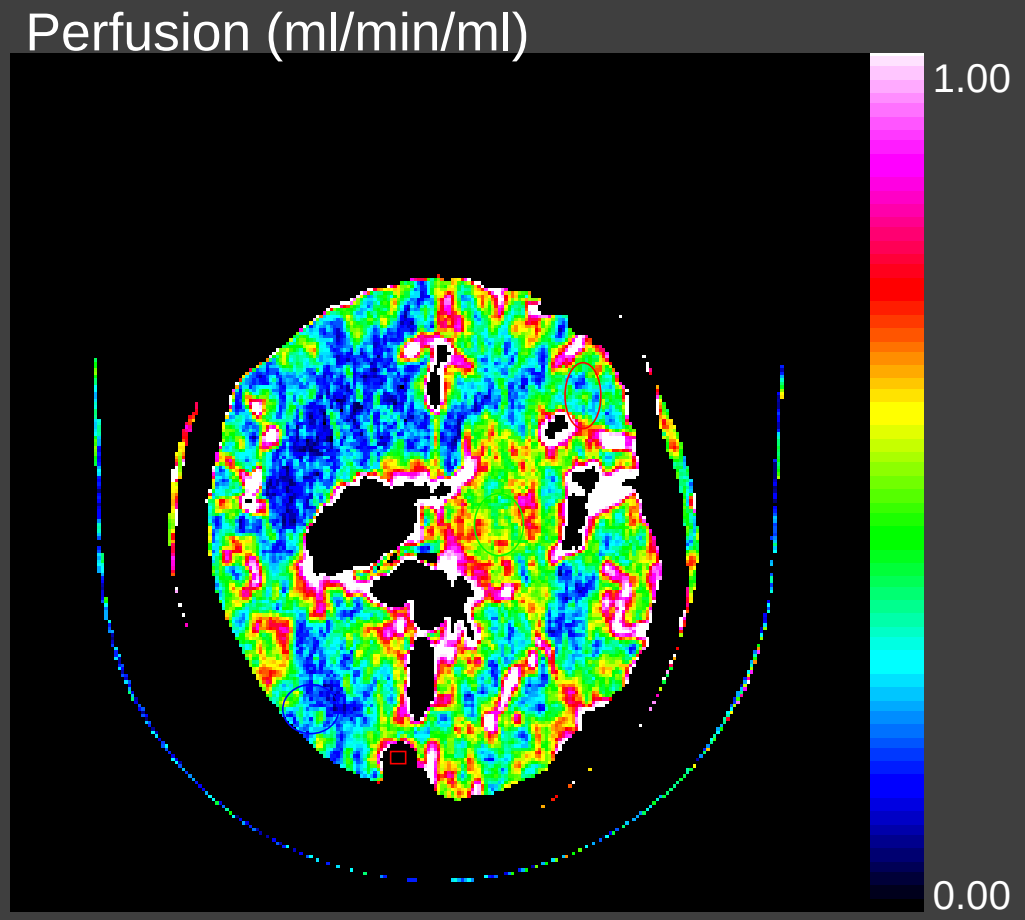
Lancet 1991; **337**: 643–45

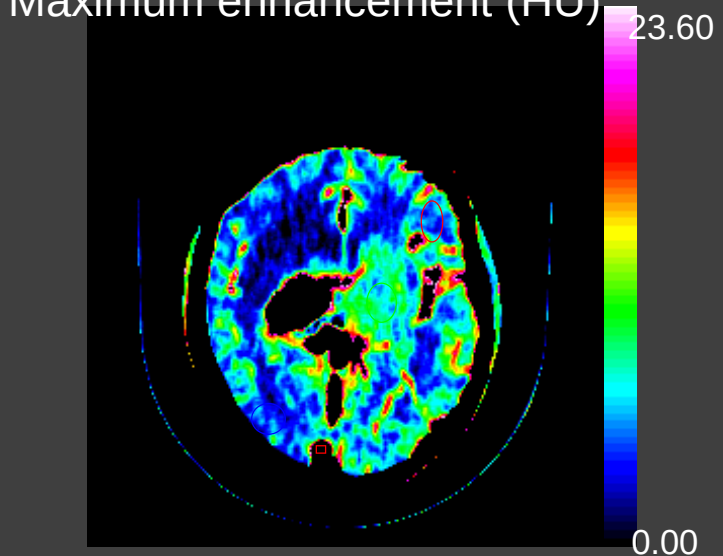
Tissue perfusion can be measured by means of dynamic computed tomography (CT) by adaptation of a nuclear medicine data-processing technique.[1,2] A rapid sequence of

Alternative approaches

- Mullani-Gould Peak Method
  - $F = {C(t_{max})}/{\int_0^t C_a(t)dt}$
  - Similar approach to maximum gradient but requires removal of recirculation
- Deconvolution / constrained convolution
  - More susceptible to noise
  - Improved by additional time points (-> increased dose)

Example - brain perfusion

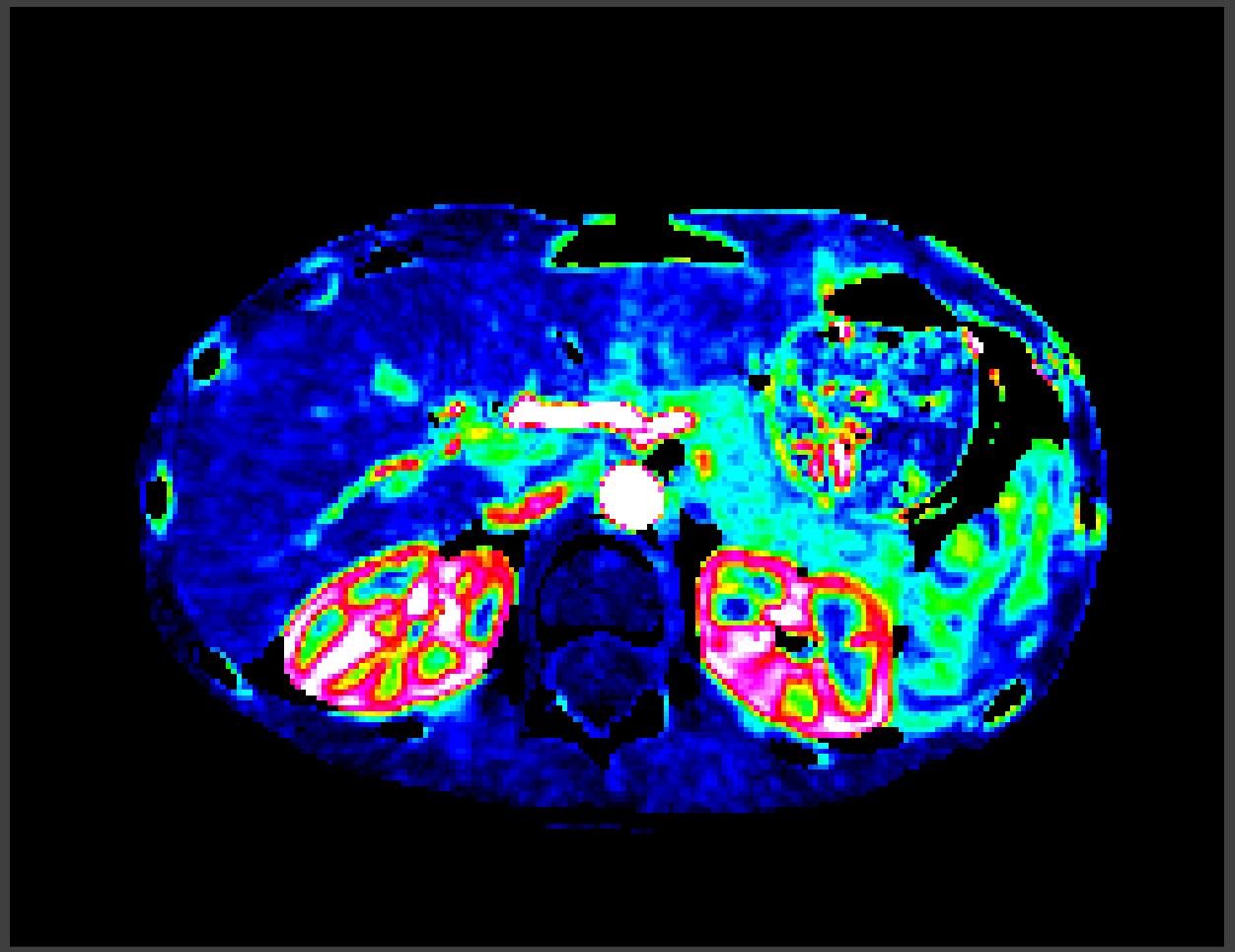




CADRAN

TEXRAD

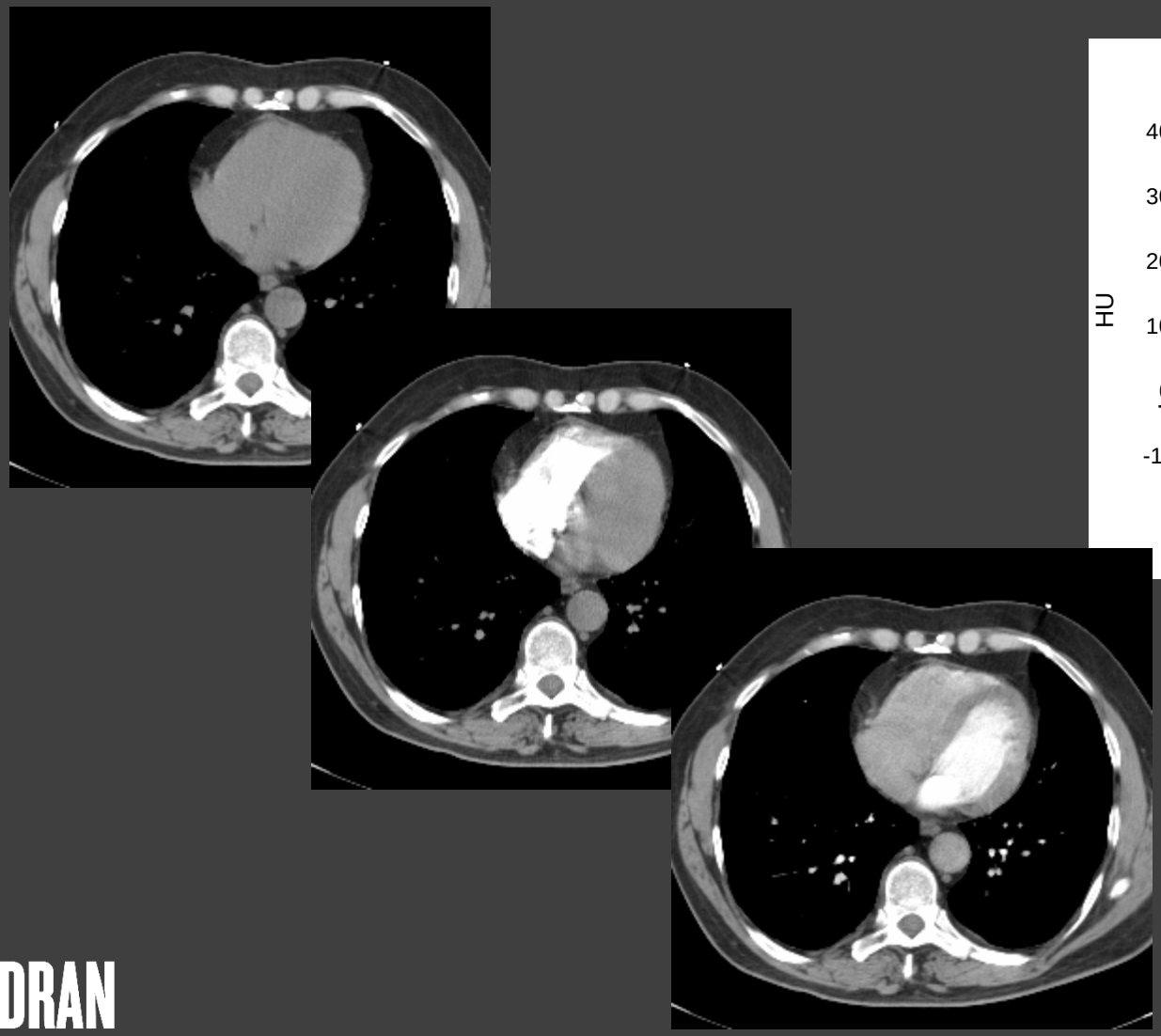
Example - abdominal perfusion

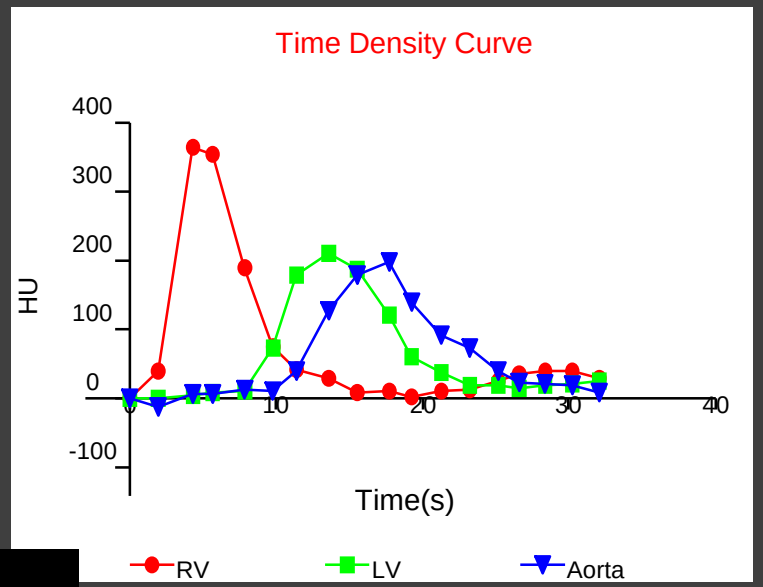


CADRAN

TEXRAD

Example - myocardial perfusion

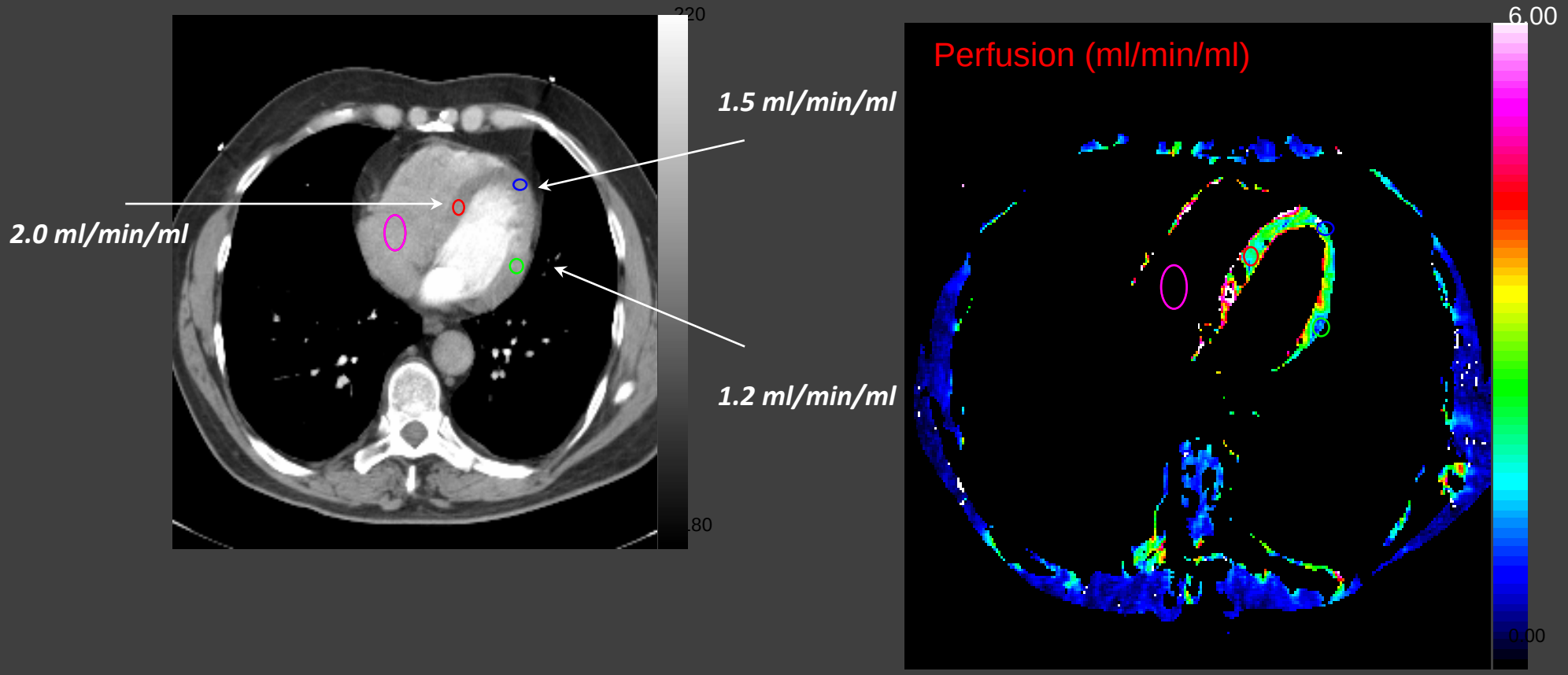




CADRAN

TEXRAD

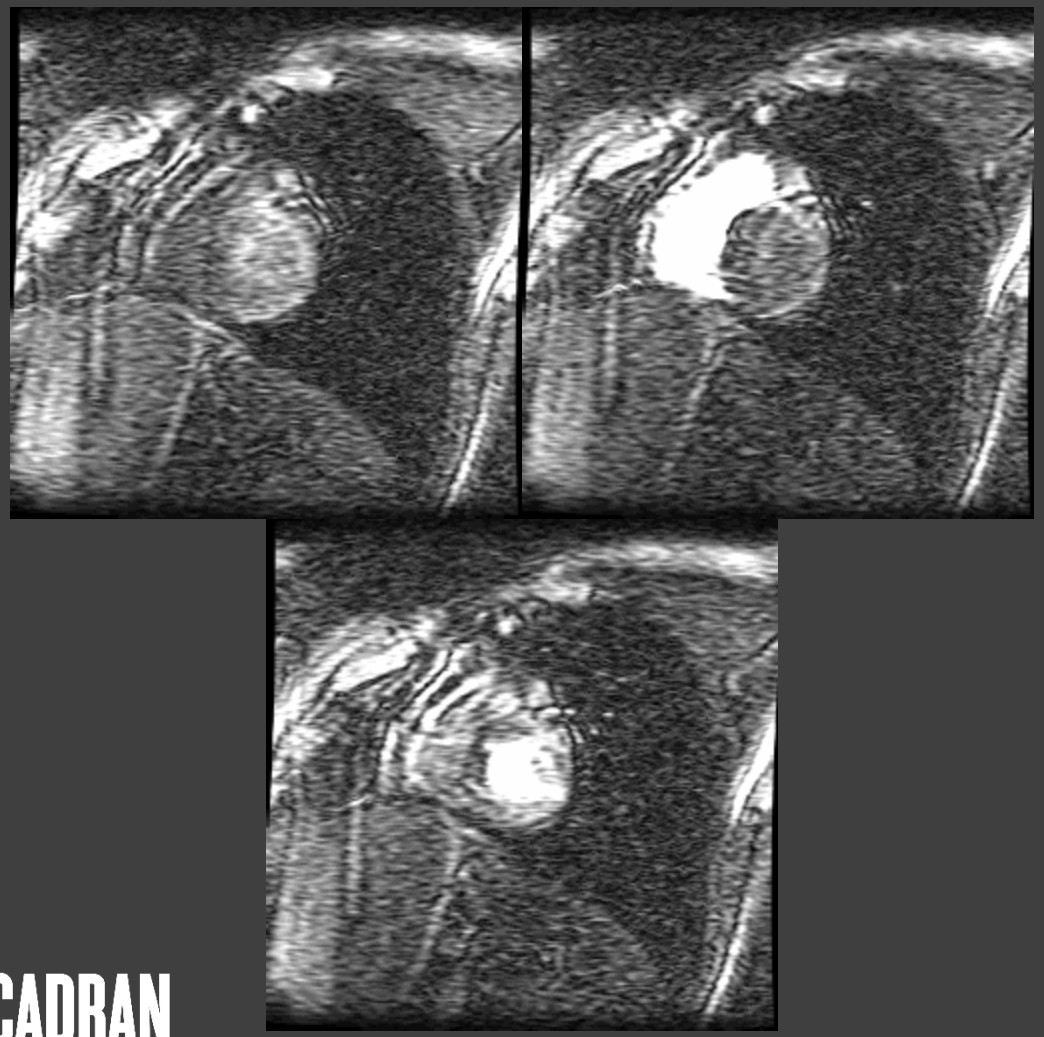
Example - myocardial perfusion

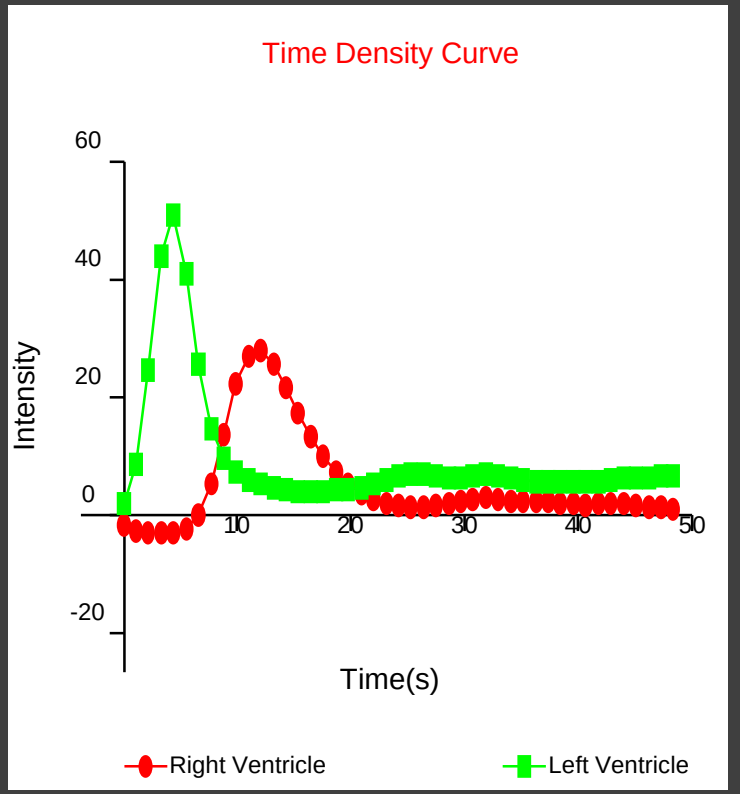


CADRAN

TEXRAD

Example - MR perfusion

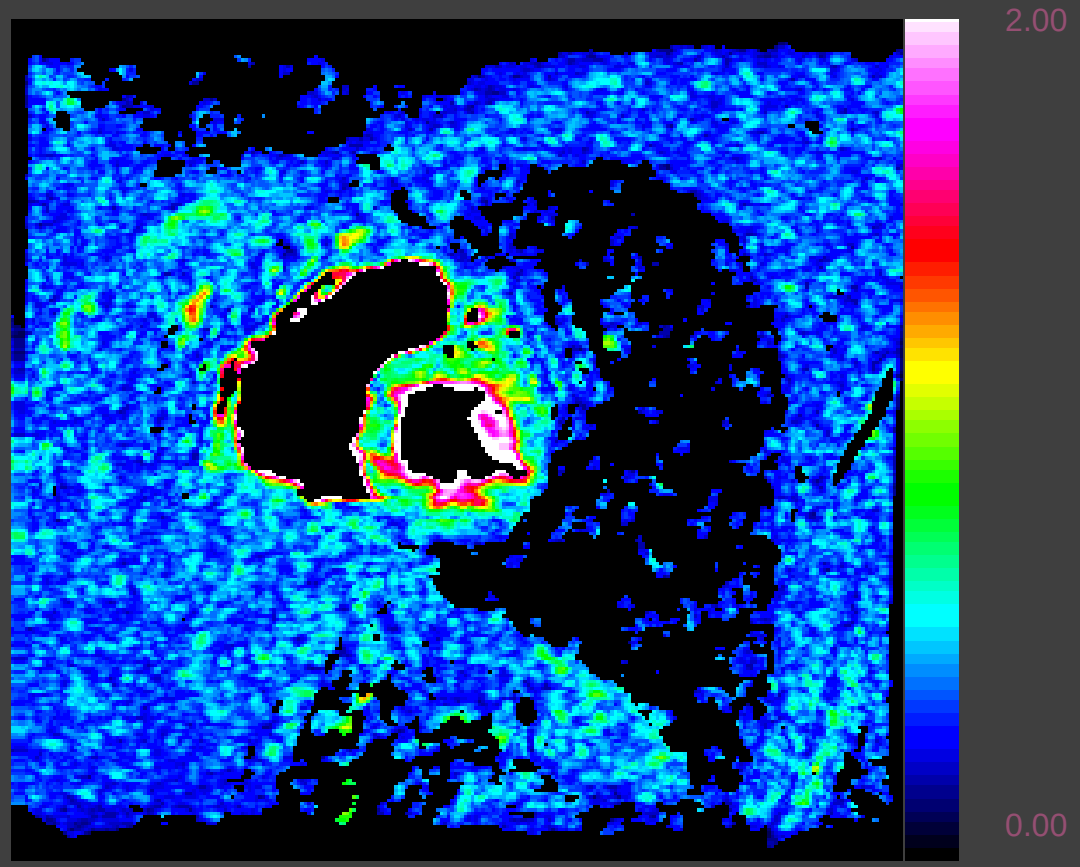




CADRAN

TEXRAD

Example - MR perfusion



CADRAN

TEXRAD

CT DCE – acquisition and performance

1991

- Single slice acquisition
  - 512x512 pixels per image
  - 5mm slice
  - Rotation time – 2s
  - 10 – 20 time points
  - < 10MB Storage
- Typical desktop CPU
  - 486 @ 33MHz – 0.05 GFlops
  - < 8MB RAM

2016

- Multi-slice detectors
  - 512x512 pixels per image
  - 64 - 192 slice, 4-16cm "slab"
  - Rotation time – 250s
  - 20 – 40 time points
  - < 6GB Storage
- Typical desktop CPU
  - I7 - > 100 GFlops
  - > 8GB RAM

CT DCE – processing

1991

- Transfer the data
- Identify inputs
- Create time-density curves
  - For region of interest
  - For pixels
- For each time-density curve
  - Clean-up data
  - Calculate derived parameters
- Present output

2016

- Register the images
  - Non-rigid deformation
  - Breathing
  - Cardiac motion
  - Movement
- Segmentation
- Constrained convolution / deconvolution

CT DCE – why is it still here?

- Simple to implement
- "Technologically robust"
  - Source images unchanged
  - Improvements extend applicability
- Sources of error
  - Noise
  - Motion
  - Calibration (contrast response)

- Is it "perfusion"?
  - Assumptions break down "gracefully"
  - Consistent in regions with identical input

Conclusions

- Big data – what is it?
  - >1GB per study
  - < 10 “values” per study
- Ideas often precede the capability
- Simplicity and reproducibility are important
- Adoption of new ideas takes time and patience