Methods En Vogue: How Have They Fared Over Time

Perfusion imaging: brain & body

Prof. Anwar R Padhani. Mount Vernon Cancer Centre, London, England

anwar.padhani@stricklandscanner.org.uk

Perfusion MRI plays key roles in cancer patient management

- To screen for breast cancer in high risk patients
- To improve detection/characterisation/delineation of lesions within organs
- Monitoring response to treatment
  - Conventional treatments (chemo/hormones/RT/physical treatments)
  - Novel biological treatments including antiangiogenic/vascular targeting agents
- Assess residual disease after definitive treatment
  - Scar vs. necrosis vs. active tumor
- Detect recurrence when tumor markers become positive

Problems of perfusion imaging – too many techniques/too many methods of analysis/no consensus on what works best and in what situation

- Qualitative - curve shape of signal enhancement data
- Physiological indices - from contrast medium concentration changes using pharmacokinetic modeling
  - DCE-MRI – standard Tofts', extended Tofts', St Lawrence & Lee, Shutter speed; many more
- Model-free indices that describe one or more parts of enhancement curves
  - Wash-in, wash-out gradients, max amplitude, time to peak etc
  - Area under signal intensity or [Gd] curve (IAUGC)
  - Hepatic perfusion index (HPI = arterial flow/total flow) for liver tumors with dual blood supply

What do kinetic parameters mean biologically? Let's take the example of Ktrans

- Ktrans meaning changes according to flow & leakiness of underlying vasculature
  - Ktrans meaning varies by anatomic location and therapy status
- Ktrans value changes according to complexity of model*
  - Adding a vp (fractional blood volume) lowers Ktrans values

- Ktrans meaning changes according to AIF used in high leakage environments like tumors
  - Weinmann (often used with standard Tofts; no vp term) → dominated by perfusion>permeability
  - Parker recirculation (often used with extended Tofts; vp term present) → reflects permeability>perfusion

AIF: population versus measured, which one is best?

- Measurement of input function at the level of the tumor (local AIF) is not yet possible to do directly
- Measure from artery in FOV (measured AIF) – needs 2 injections
- Derive from a reference tissue (muscle) (reference tissue AIF)
- Assume normal values (population average or pooled AIF)
  - Bi-exponential : Weinmann, Fritz-Hansen, Modified Fritz-Hansen, Femoral artery
  - Complex wave forms: gamma/cosine then bi-exponential/Parker recirculation/dual source inputs
- Important to match data acquisition strategies to the proposed AIF usage; but this affects reliability of kinetic parameters
- An AIF that enables a curve to fit well with low residuals in one clinical situation, doesn't mean that the same AIF will perform well when the situation is changed (eg, tumor pre- & post therapy)

Do we need quantitative DCE-MRI analysis in oncologic clinical practice? Are the advantages worth it?

- Disadvantages
  - Data acquisition and analysis is more complex
  - Confusion on the biologic meaning of kinetic parameters
  - Too many models – do we need them all?
  - Simple models may not fit the data observe
- Advantages
  - Biologically relevant physiological parameters
  - Independent of scanner strength, manufacturer and imaging routines
  - Enables valid comparisons of serial measurements and data exchange between different imaging centers

When do you absolutely need quantitative perfusion MR imaging?

- Validation: establishing the usefulness of DCE-MRI in a specific clinical area
- Drug development: pharmacodynamic biomarker in early phase clinical trials
- As part of multi-parametric imaging assessments
  - Radiomics - to improve biologic understanding of heterogeneity at multiple scales
  - For integration with other biomarkers
  - Radiotherapy planning by numbers

Introducing quantitative DCE-MRI into the clinic

- Validation phase - should be quantitative
- Clinical deployment can be qualitative or semi-quantitative – keep it simple!
  - Ratios, curve shapes, scoring systems, structured reporting
- Example: multiparametric MRI in prostate cancer practice
  - Deployment into practice: ESUR 2011 guidelines recommend usage of curve shapes (for both DCE & MRSI) and descriptive analyses (Pi-RADS)

Conclusions

- Using perfusion imaging in clinical practice should not be delayed/hindered by the complexities of the techniques outlined above
- Complex quantitative analysis has roles in validation, drug development and is needed for multiparametric assessments
- Future work should now focus on incorporating perfusion imaging as part of multiparametric assessments
  - Towards improving understanding of tumor heterogeneity, including response in the era of targeted/precision medicine