Biopsies: is there such a thing as too much?

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On behalf of the CM-Path Initiative

NCRI
National Cancer
Research Institute

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Partners in cancer research

What do we mean by 'biopsies'?

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- Archived diagnostic tissue specimens that may be available for central review by experts and/or (increasingly) for translational research.
  - Resection
  - Excision/incision
  - Endoscopic/'trans'
  - Needle core +/- image guidance

- Additional tissue biopsy samples obtained specifically for research.

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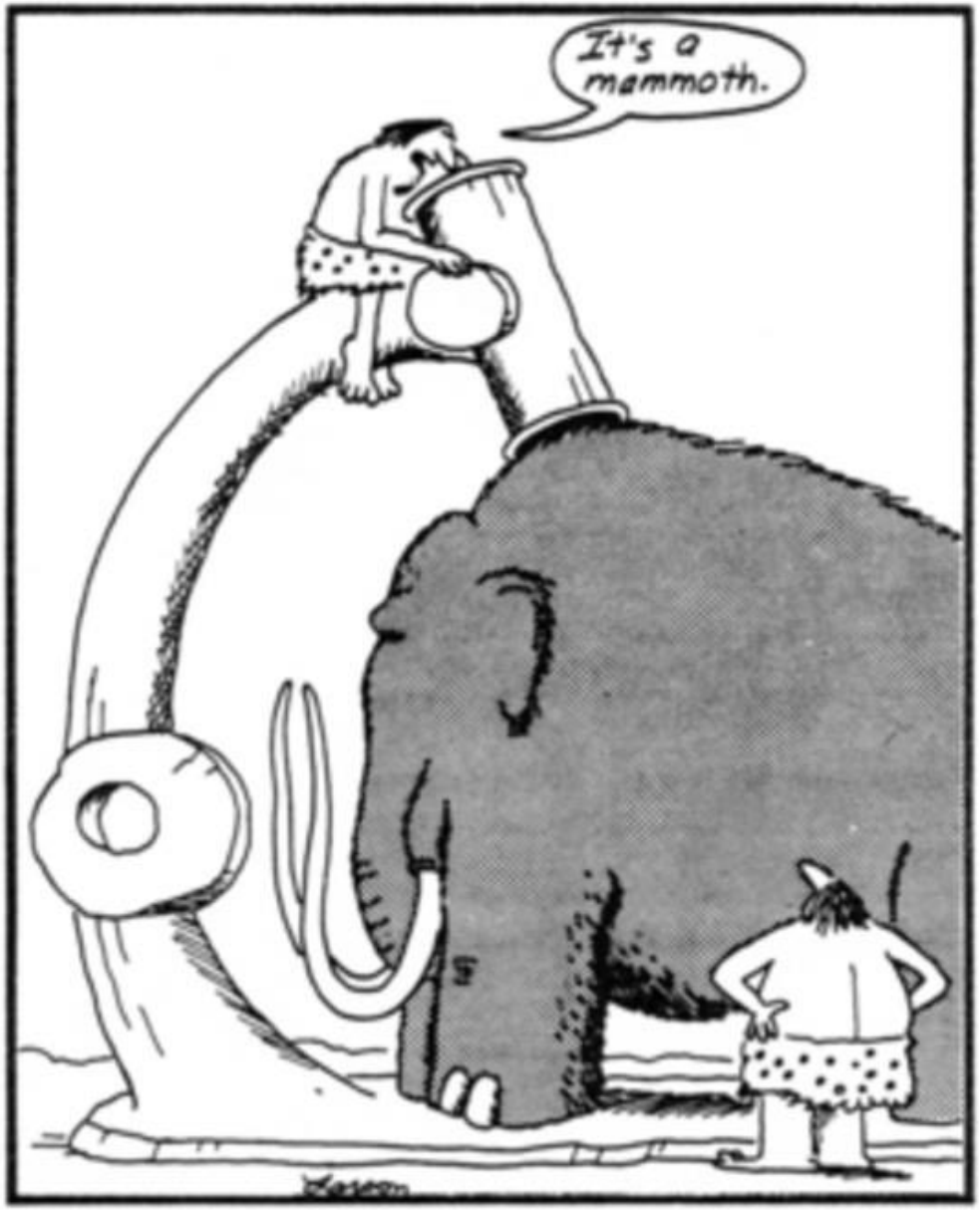

"Conventional" Microscopy

"Bench-top" Next Generation Sequencing

Tissue in paraffin wax block

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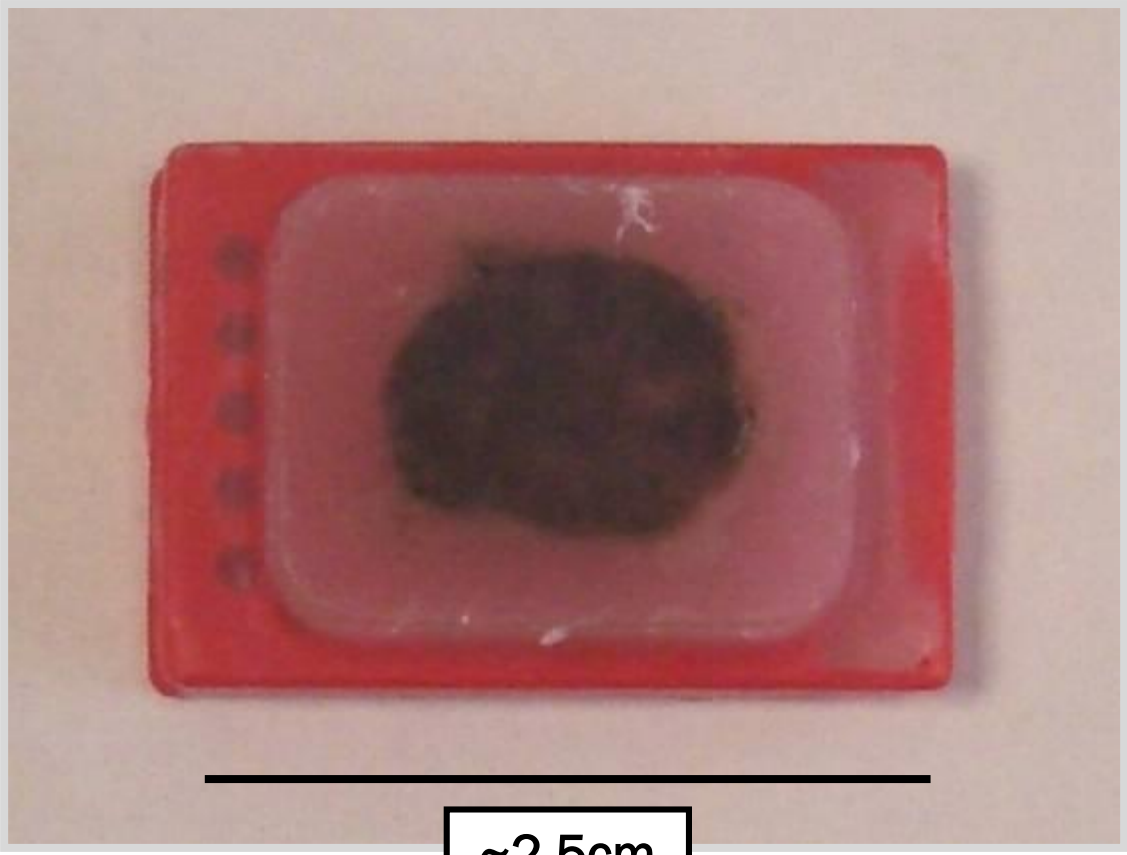

Tissue block, unstained and stained sections

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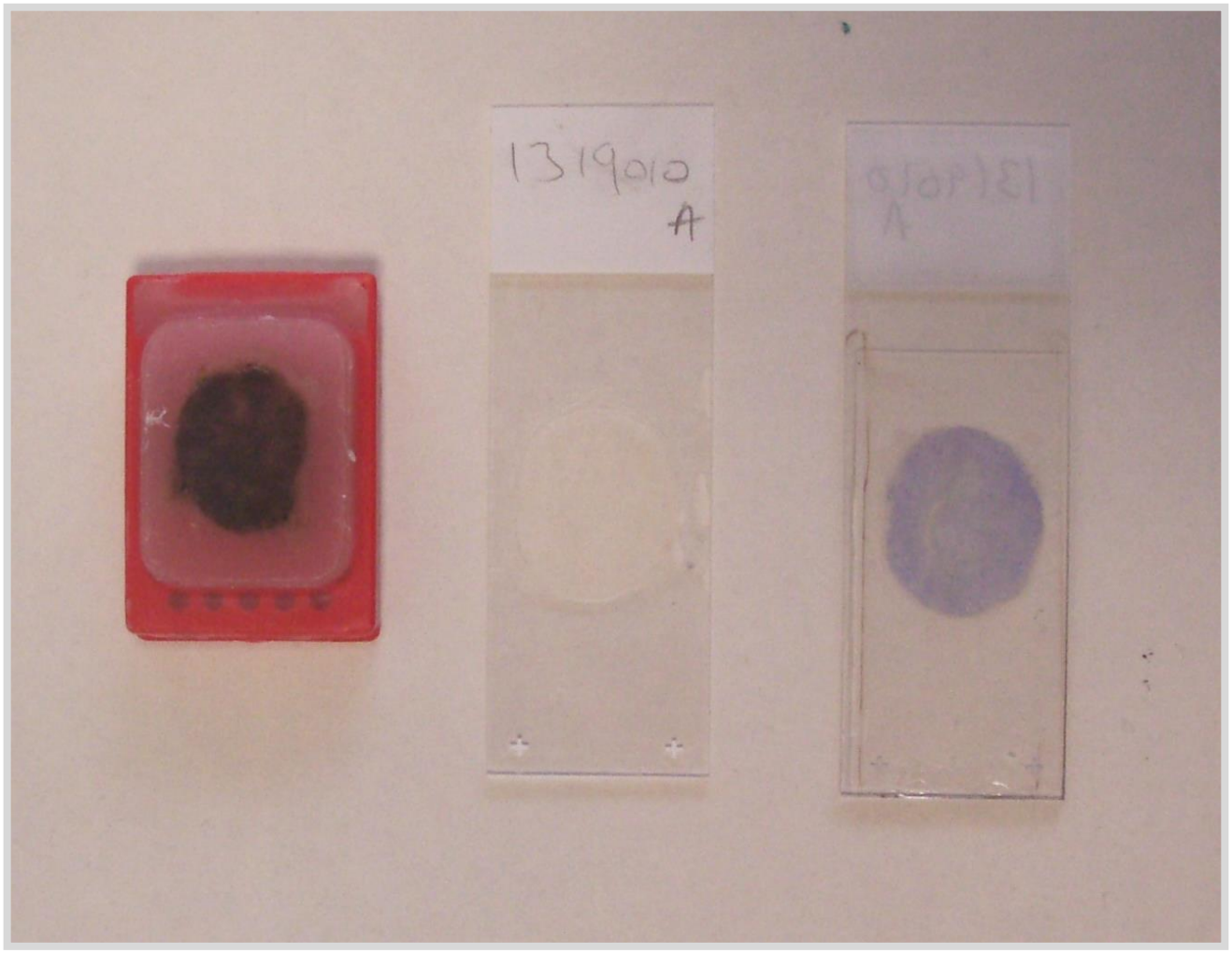

Tissue block: needle biopsy core

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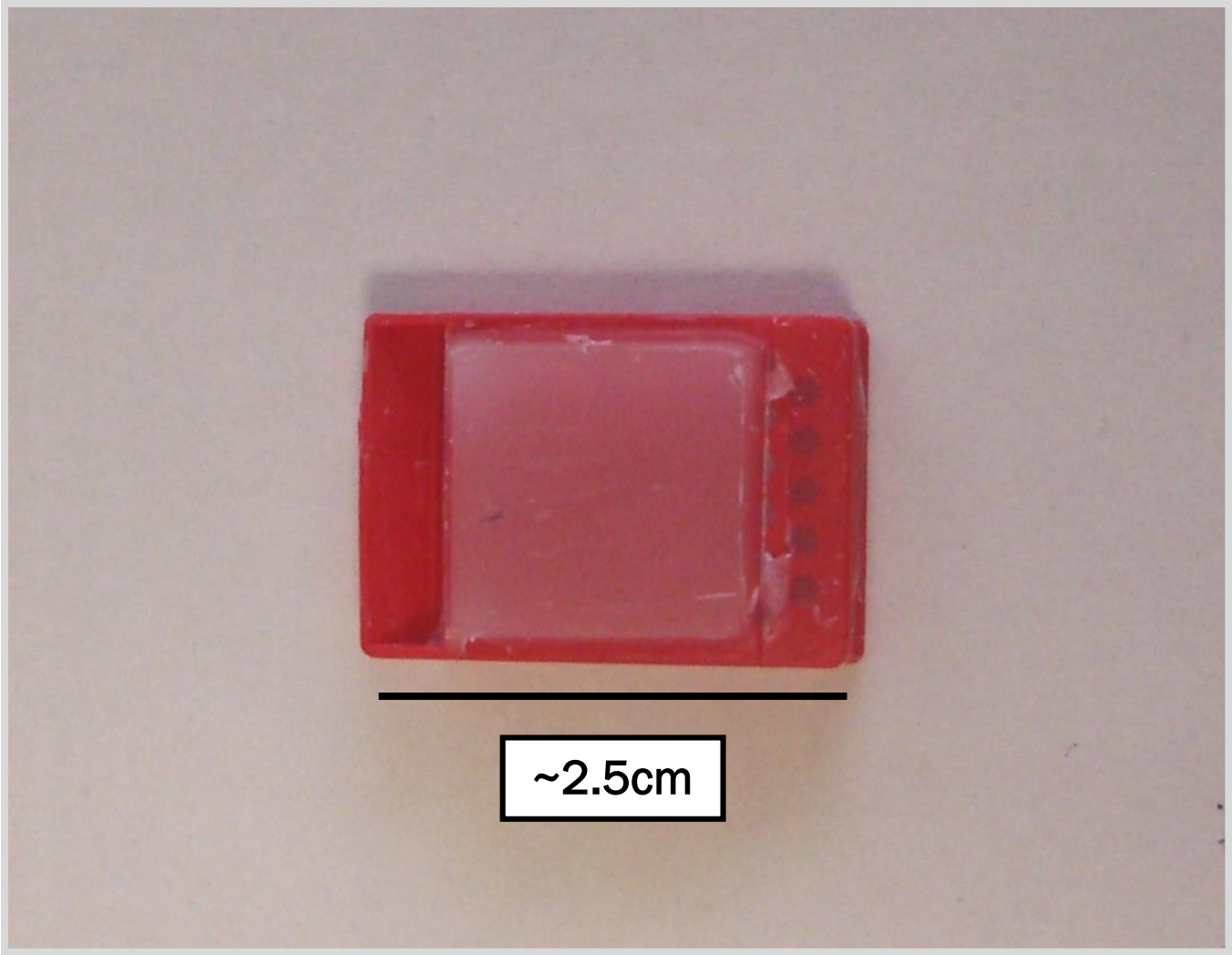

Needle biopsy core: Stained section

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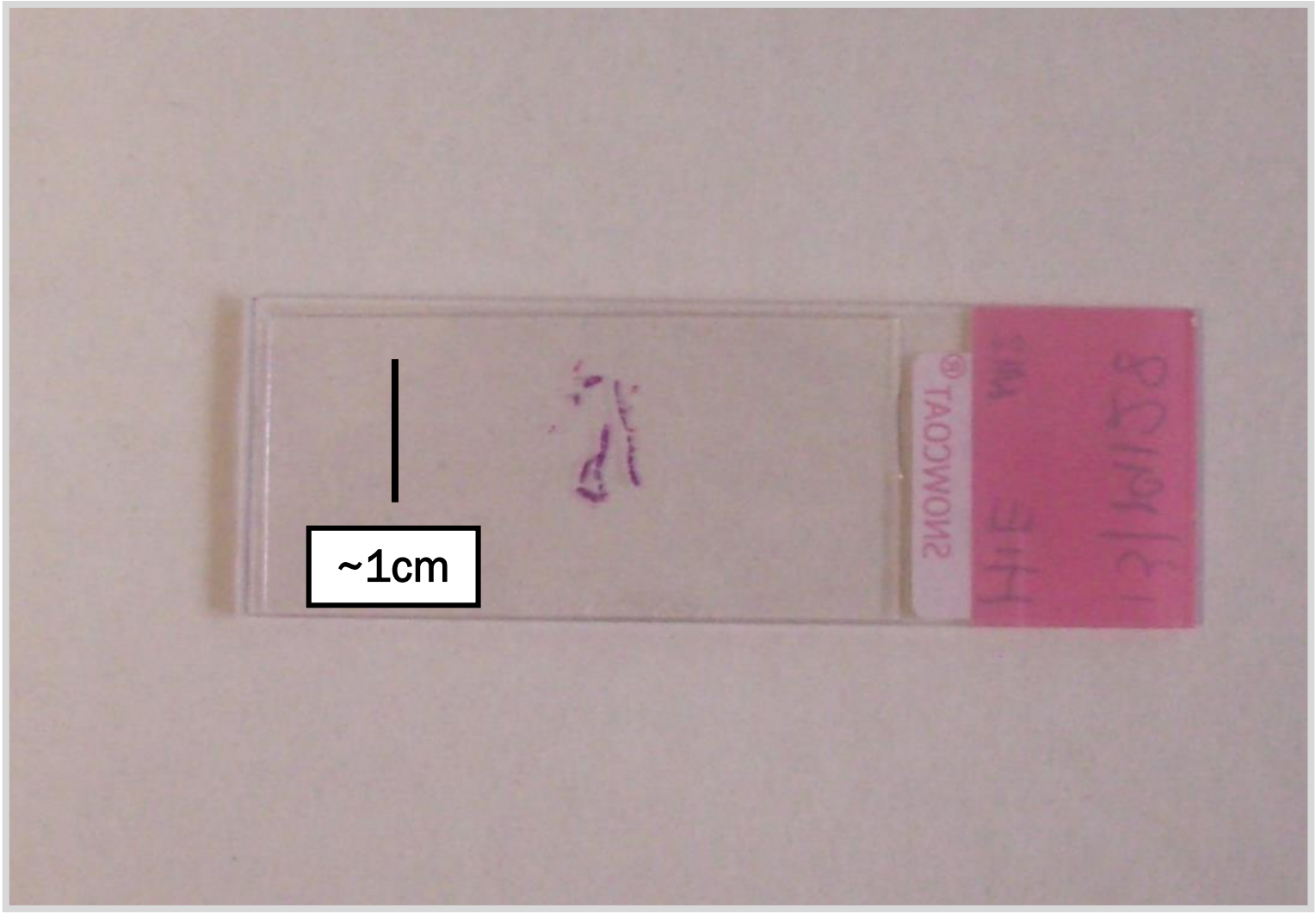

How much tissue is in a block?

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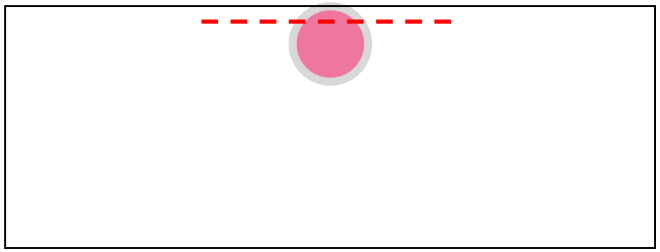

Needle core 1mm diameter

= 1000 microns (µm)

Sections 2-3 microns thick

= 300-500 sections

Tissue slice 3-4 mm thick

= 3-4000 microns (µm)

Sections 2-3 microns thick

= 1000-2000 sections

Re-cutting uses ~20 sections each time for realignment and 'trimming in'

When are biopsies needed for clinical treatment decisions?

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- Initial diagnosis
- Staging
- Confirmation of suspected relapse
- Re-staging
- Reassurance after treatment

Is tissue truly 'surplus' after diagnosis?

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- Traditionally regarded so, but things are changing…
- Particularly in cancer medicine, we need more often to return to stored blocks to test them, sometimes after many years, to look for markers that a patient may respond to a new drug.
- We may also need to compare 'old with new' in future, to predict whether a patient's cancer has changed over time and so may need different treatment.

Are biopsies taken for clinical reasons any good for research?

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- Hospital pathology departments have little influence on conditions before the tissue reaches them from the endoscopy suite or operating theatre (‘cold ischaemic time’).
- Fixation (preserving), processing (preparing for wax-embedding) and storage arrangements for diagnostic tissue samples vary widely.
- Until recently, getting the best morphology has mattered most.

Why and when are biopsies taken specifically for research?

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- Rarely at diagnosis, but small samples from diagnostic tissue may be removed for biobanking before standard pathology processing
- Additional staging samples in some clinical trials, where diagnostic needs might be met by imaging alone (tumour heterogeneity)
- Additional samples after treatment in some clinical trials, specifically to assess treatment response
- Additional samples at relapse in some clinical trials, when imaging is sufficient clinically
- Post-mortem samples; the “ultimate audit”

Biobanking for research tissue samples

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- A formal biobank aims to standardise cold ischaemia, fixation, processing and storage as far as possible.
- Frozen storage is a particular problem for diagnostic labs but operates well in biobanks – currently a better source for many studies needing high quality DNA and RNA.

Enough biopsies?

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- Patient (dis)comfort - needle core or more?
- Multiple site sampling to assess heterogeneity?
- Acceptability of post-mortem sampling?
- Capacity of biobanks?
- Capacity for data updating and handling?
- Quality of ‘exploratory’ translational research in clinical trials?

- When might enough become too much…?

How can I ensure my biopsies are used for maximum research benefit?

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- **Laboratories:**
  - Ideal diagnostic tissue handling in hospital laboratories
  - Biobank handling
  - Databases for sharing samples and information
- **Patients:**
  - Provide broad consent and maximum information
  - Don’t walk away; keep consent updated
  - Consider giving additional blood/mouth swabs etc.
  - Be a ‘walking donor’
  - Consider post-mortem donation

Some practicalities

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- Genuine ‘surplus’ can be ensured for some, larger specimens by taking extra tissue blocks at the outset.
- To speed up later retrieval, these can be flagged in the pathology computer system as ‘available for research’.
- This saves a pathologist having to review all the histology slides to find a suitable block when a research study requires one.

Some practicalities

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- Even better, such pre-identified blocks can be handled and stored specifically to maximise research potential (e.g., use non-standard fixatives +/- store in a fridge or freezer long term – this is too expensive to do for all our 'routine' blocks).
- Most pathologists are sub-specialised; engage those linked to your MDT to help you with all of this.