Requirements for good tissue microarray (TMA) results

- Thick donor tissue blocks
  - At least 2 mm
  - Best if $\geq$ 3mm
- Guide slide must represent the last section cut from the block
- Selection of target tissue most likely to be present through full thickness of the block
- "Tight" circling of targets required

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Use of histologic sections that are not representative of the cut surface of the block, and imprecise circling leads to the missing of target tissue, due to the "blind" nature of tissue core sampling during the TMA manufacture.

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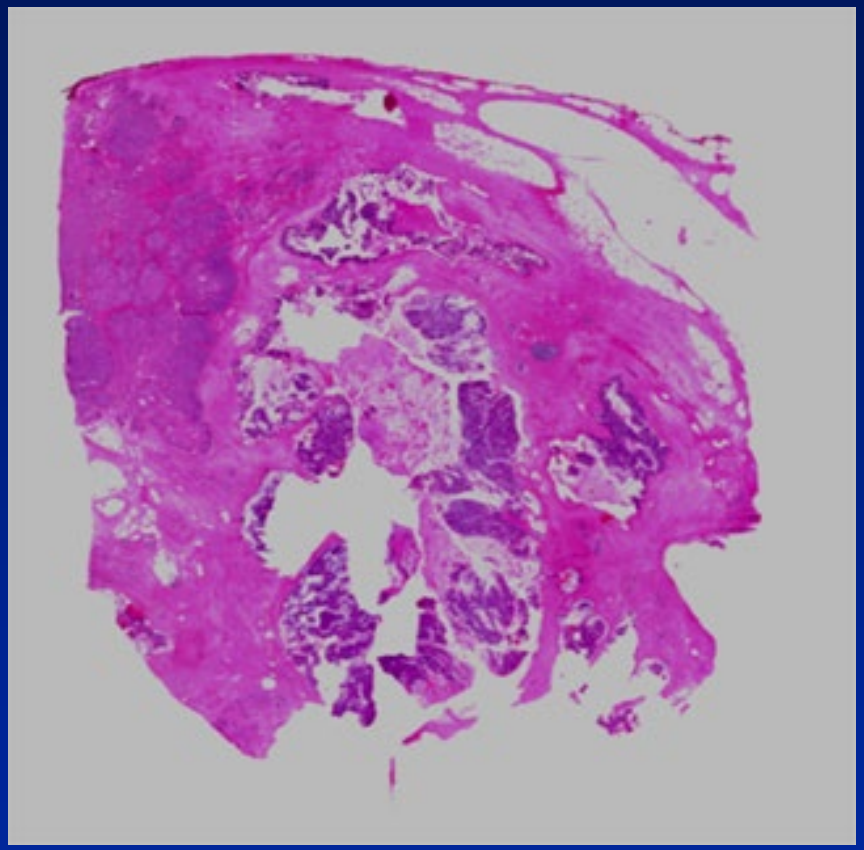
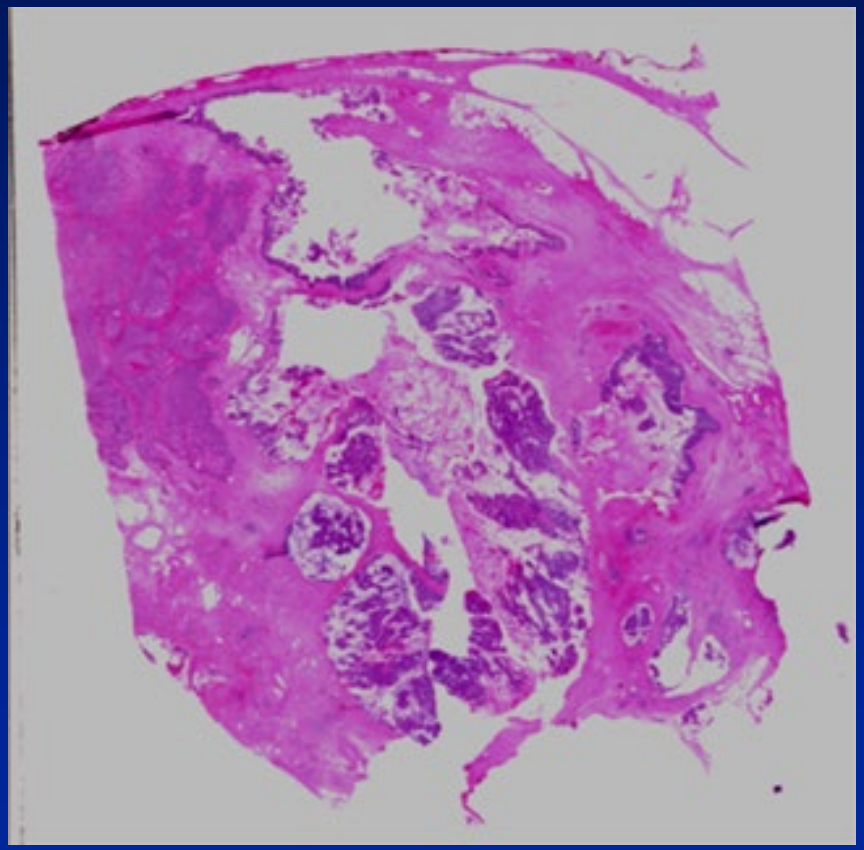
Tissue architecture changes with depth of sectioning





Tumor with solid and cystic components: histologic sections taken from different levels of the block. Note in particular that the cystic areas and the edges of the solid tumor change in position within the tissue.

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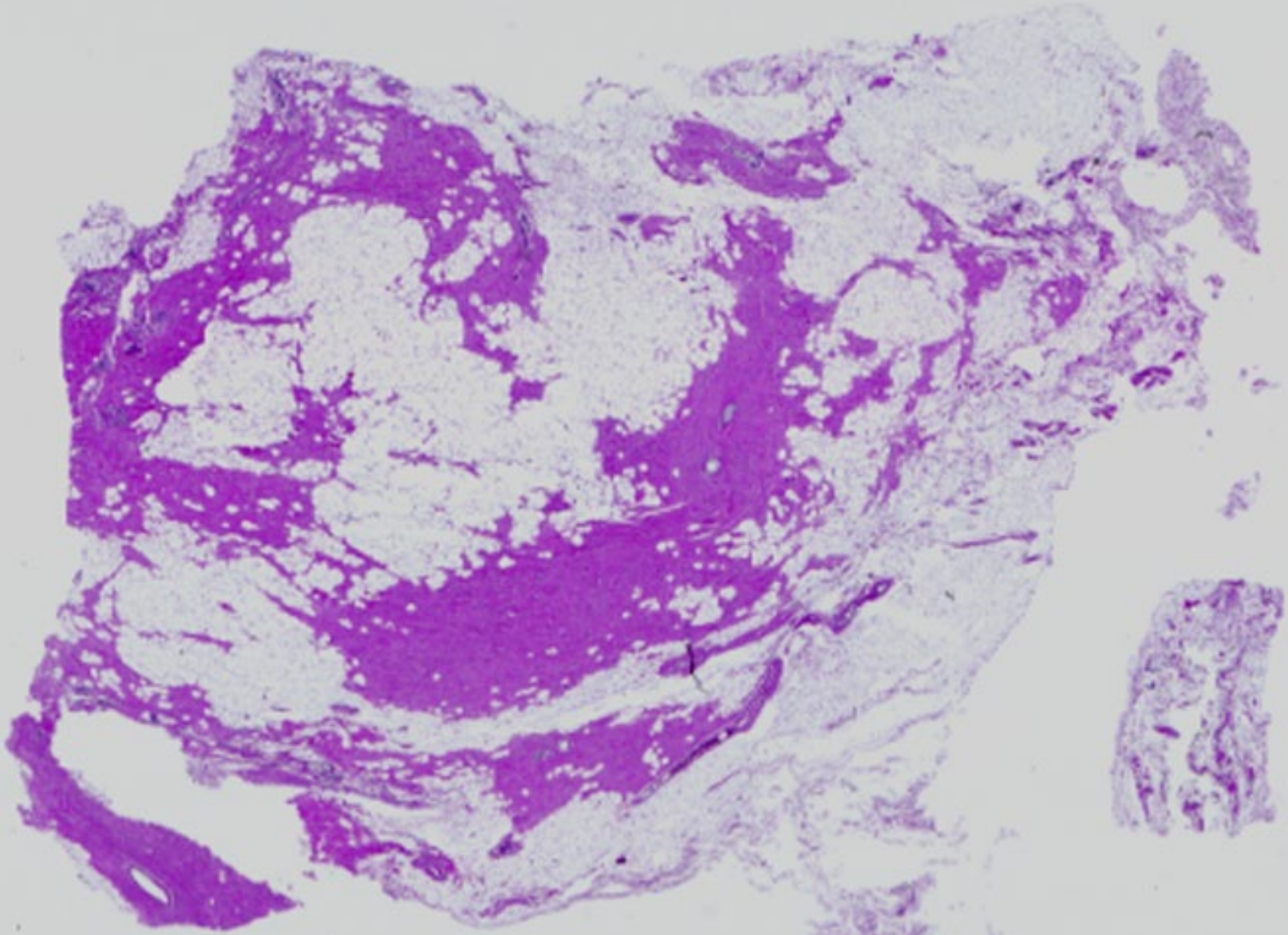

Section of breast tissue: A heterogeneous population of adipose, fibrous and epithelial structures.

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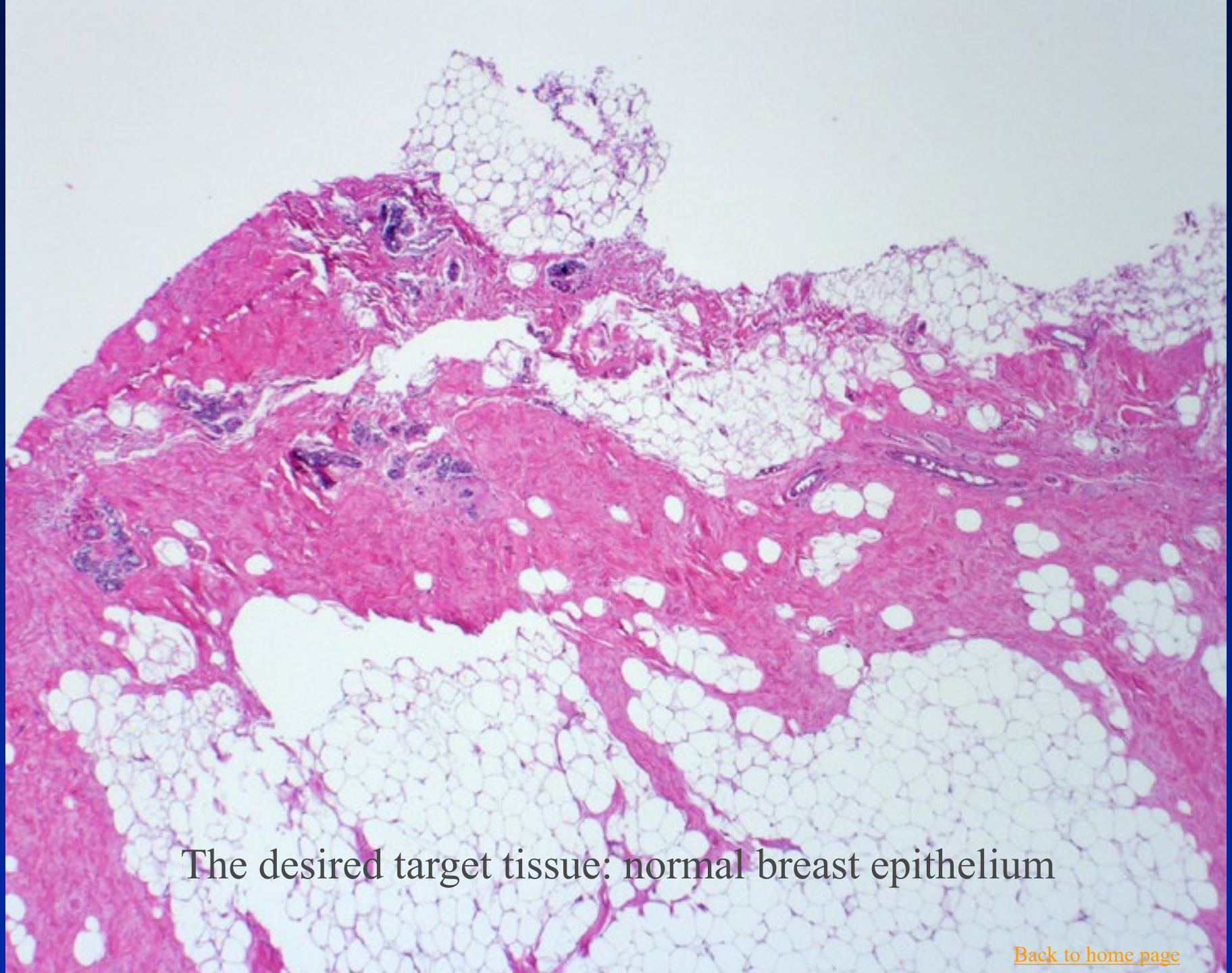

The desired target tissue: normal breast epithelium

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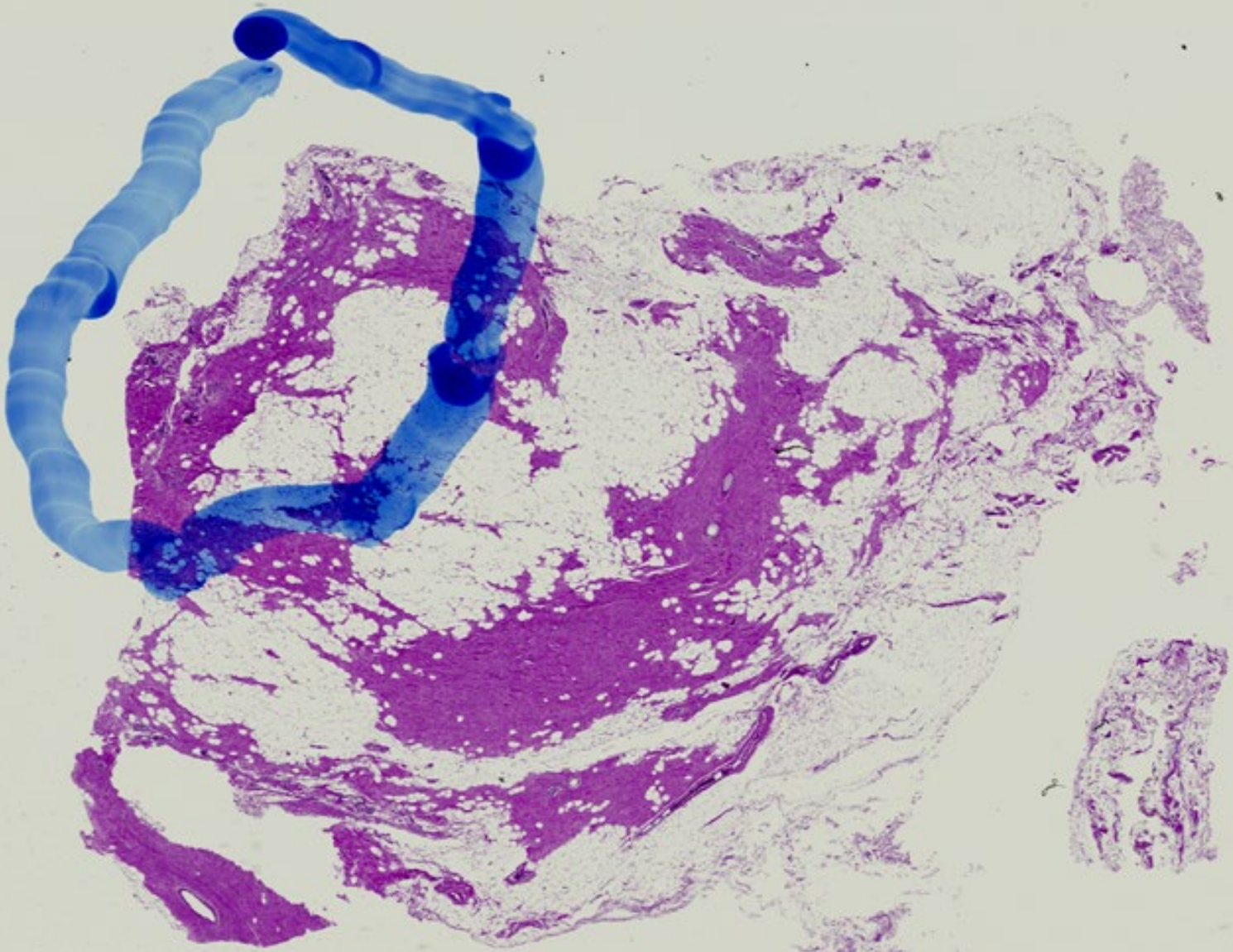

Imprecise circling may lead the maker of the TMA to miss the target tissue.

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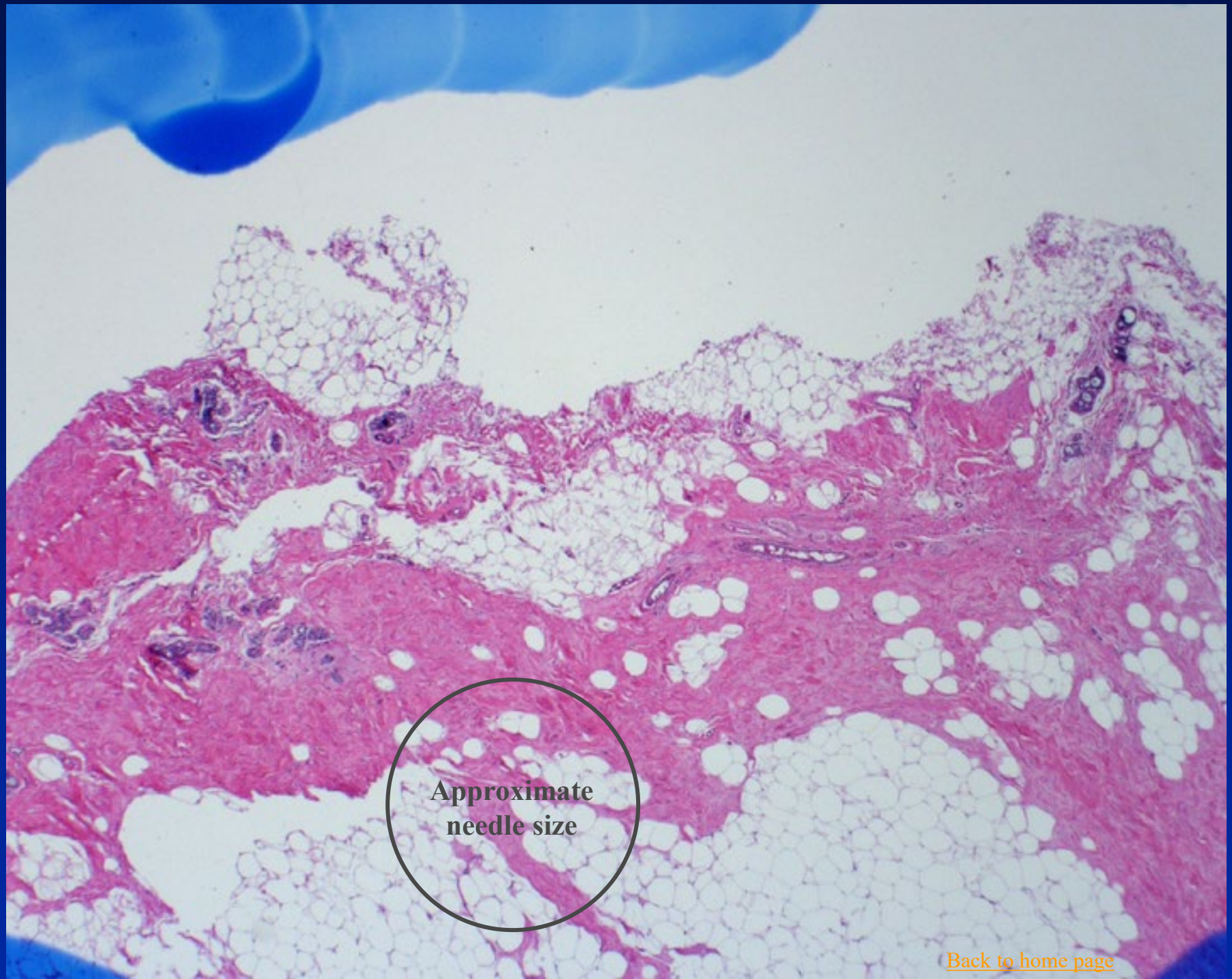

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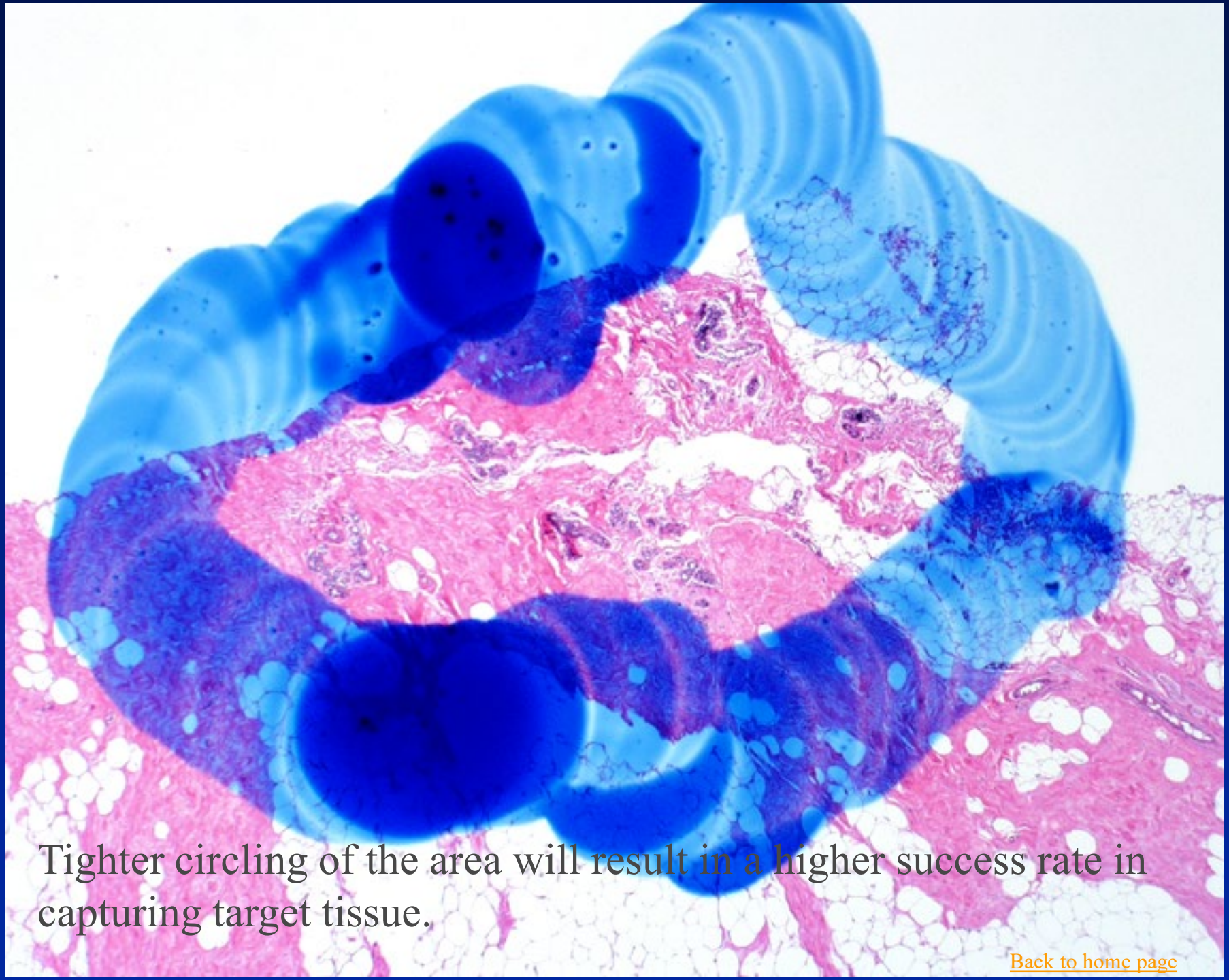

Tighter circling of the area will result in a higher success rate in capturing target tissue.

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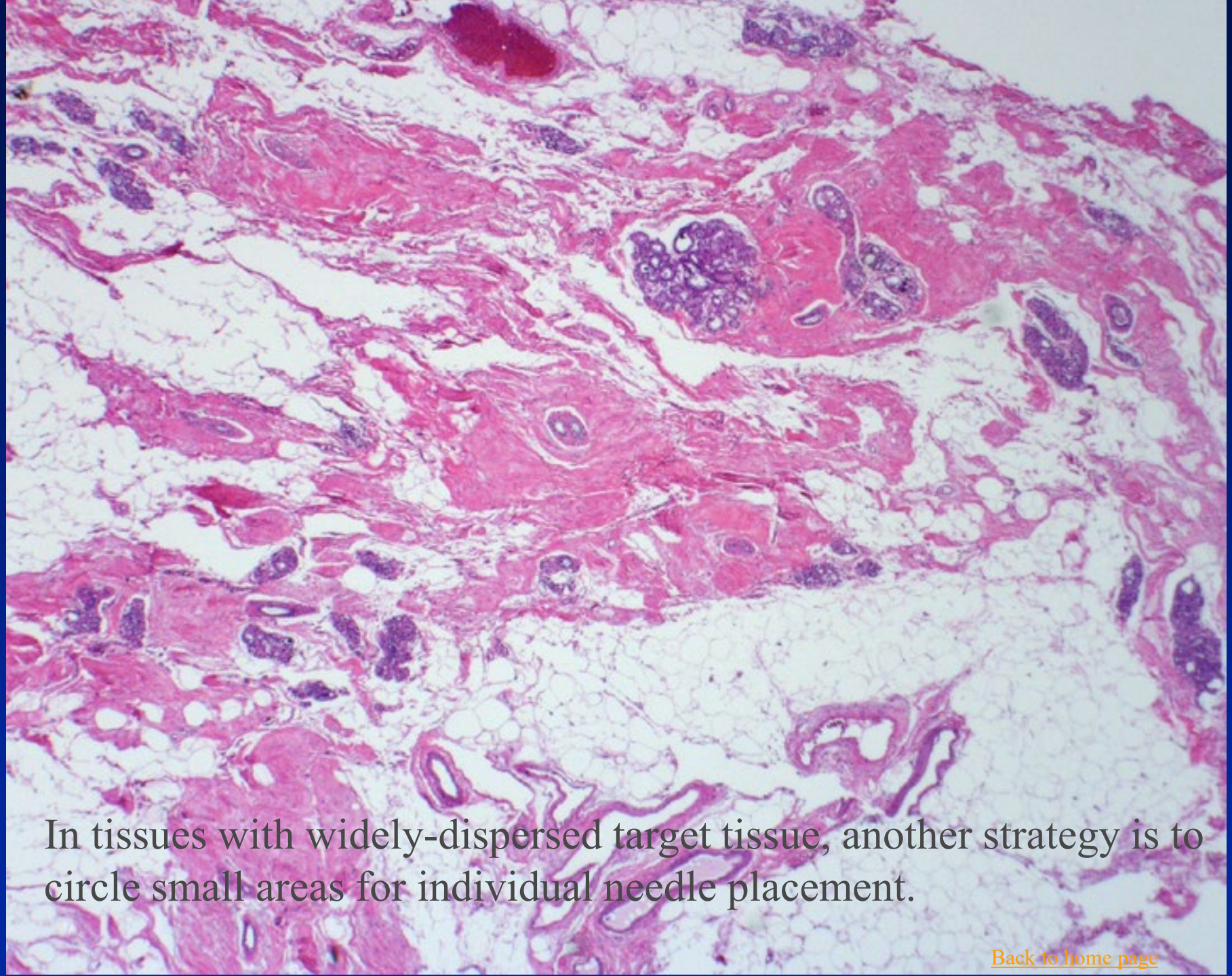

In tissues with widely-dispersed target tissue, another strategy is to circle small areas for individual needle placement.

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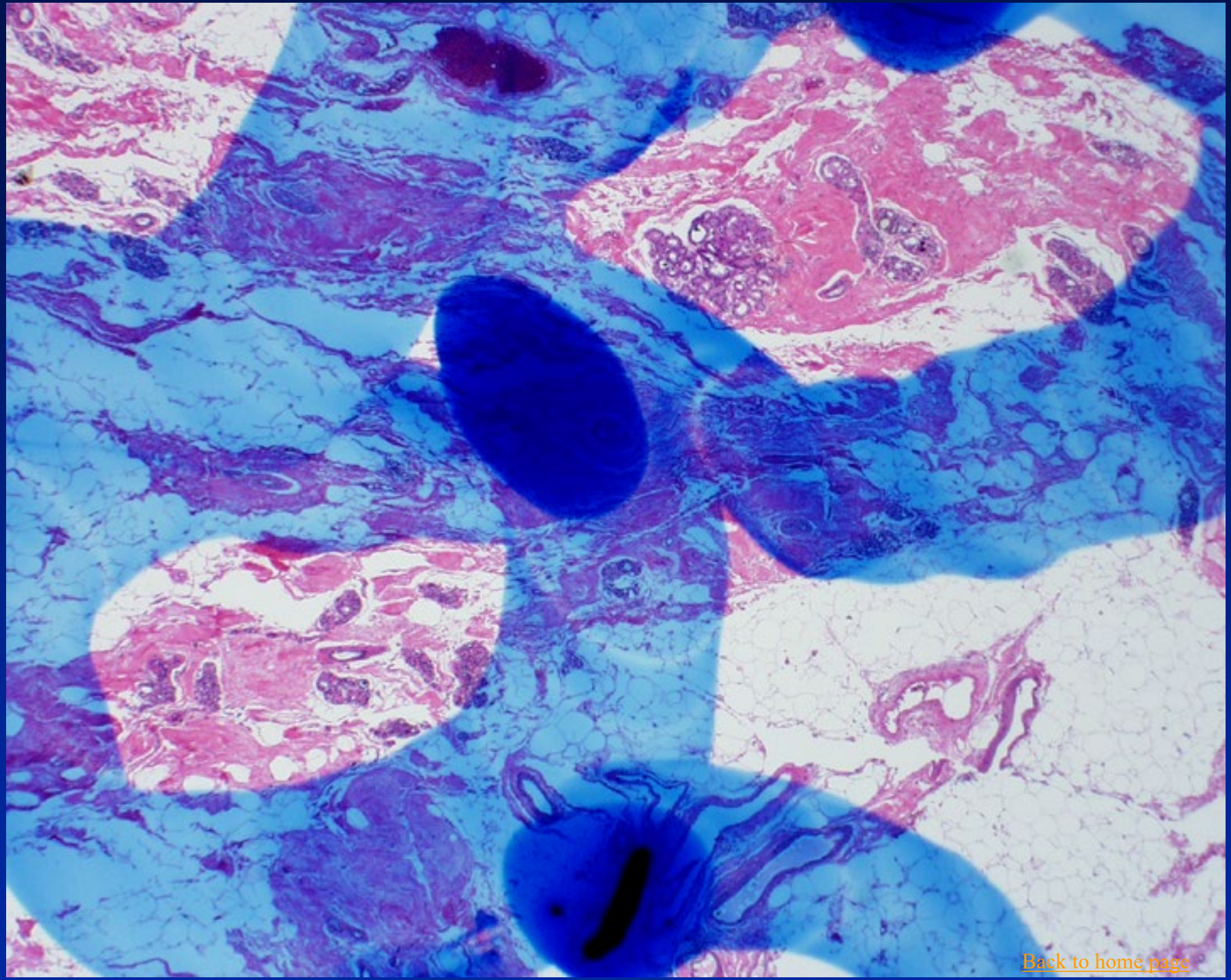

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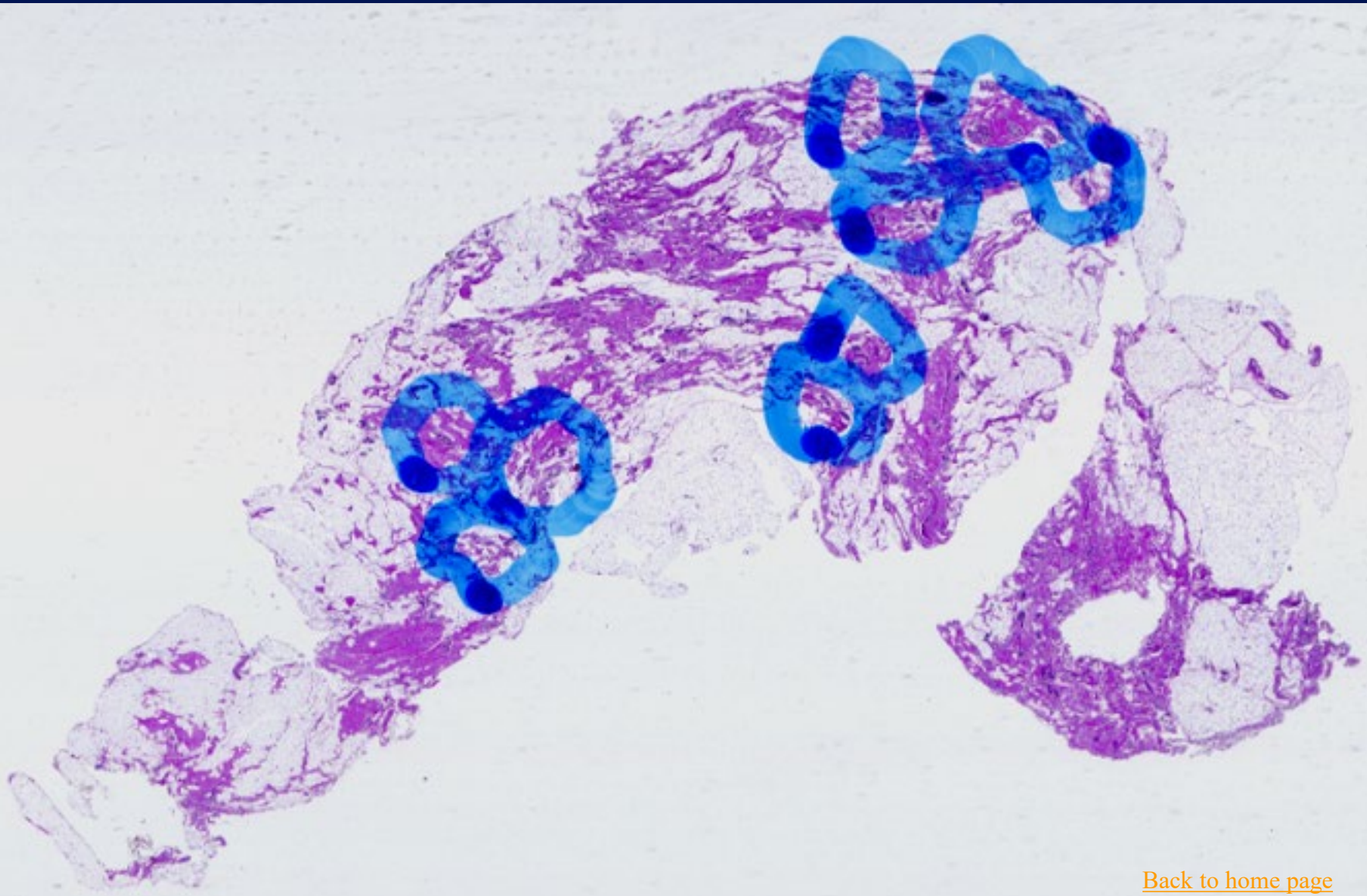

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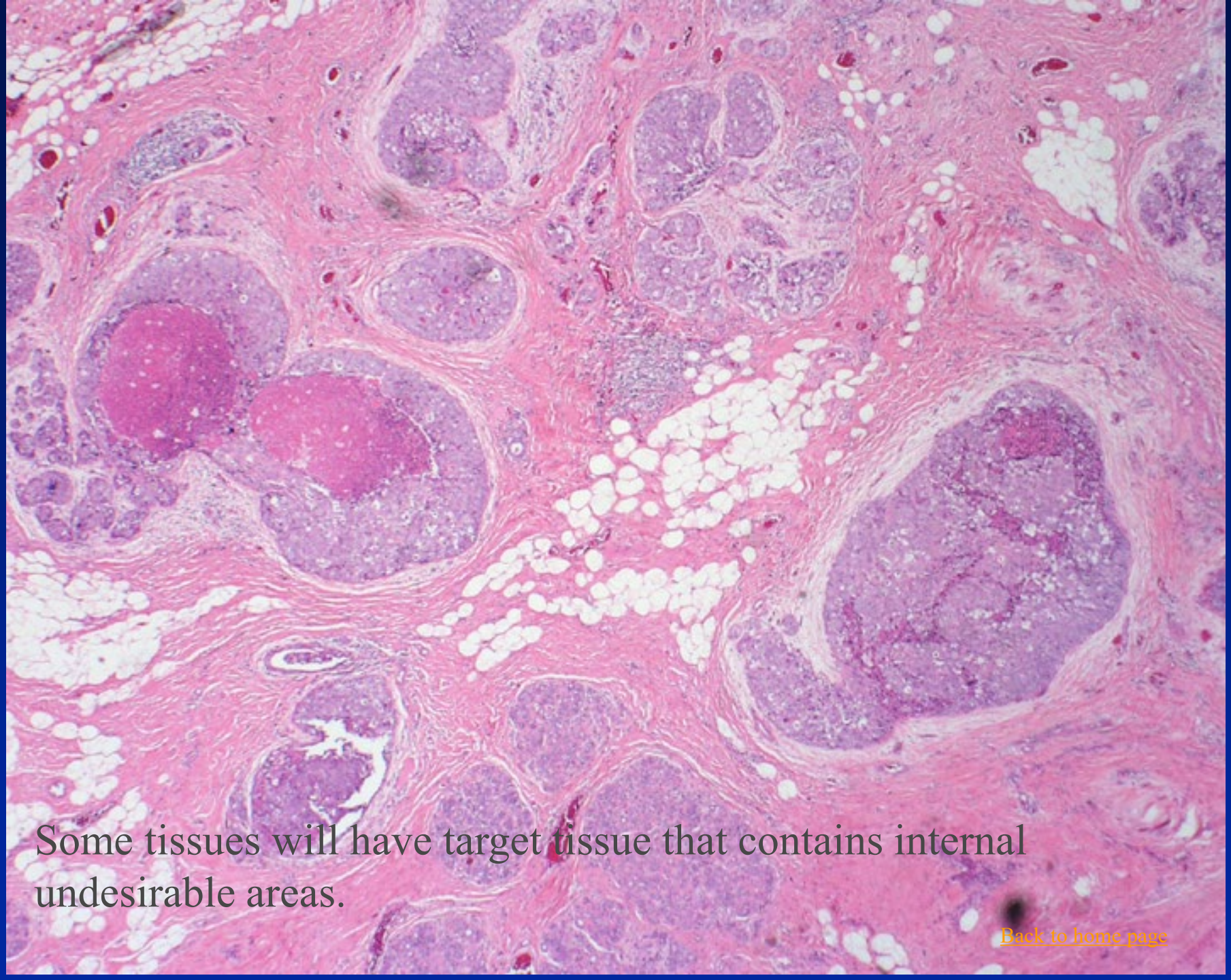

Some tissues will have target tissue that contains internal undesirable areas.

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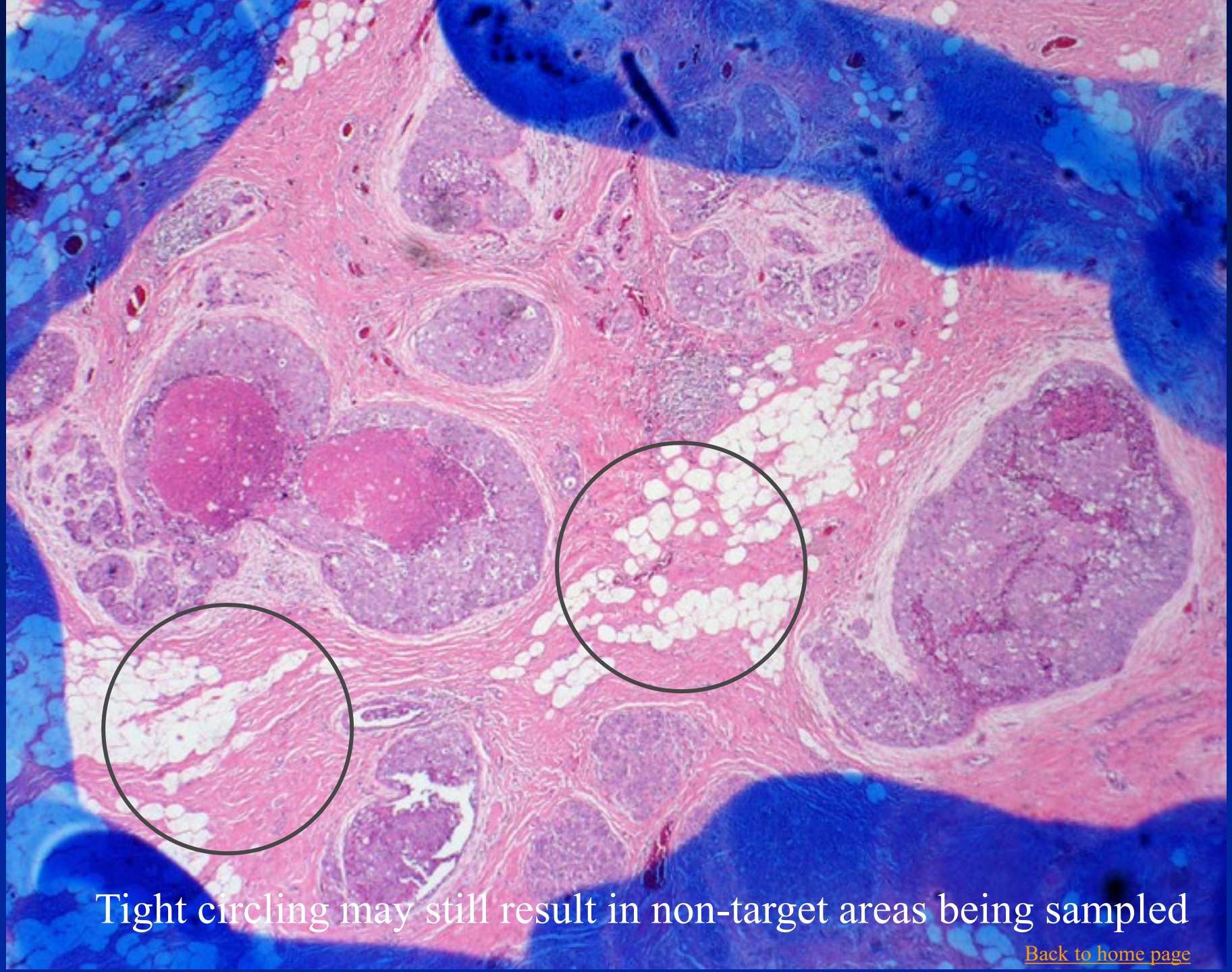

Tight circling may still result in non-target areas being sampled

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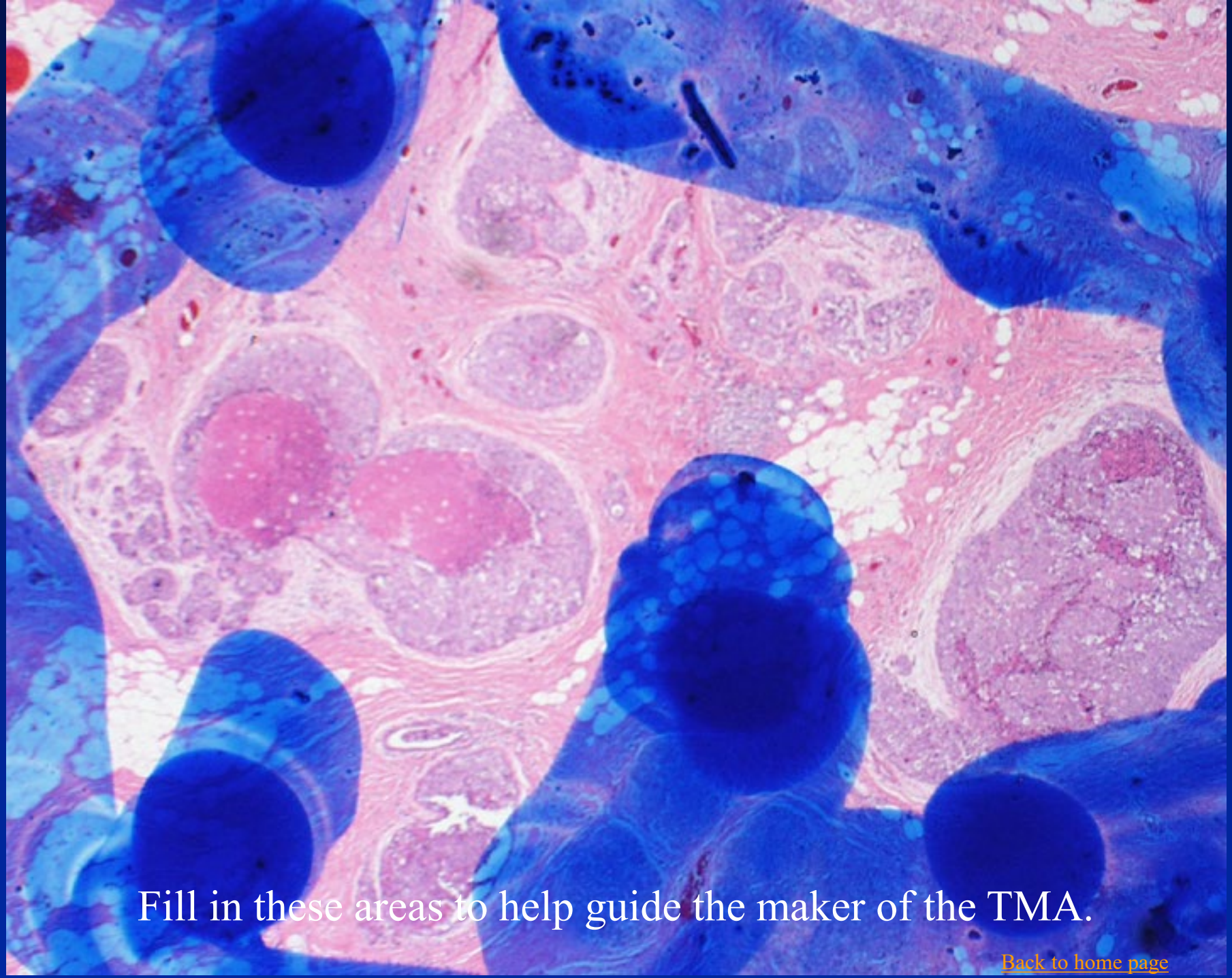

Fill in these areas to help guide the maker of the TMA.

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Problems inherent to tissue

- Tissue targets smaller than the thickness of the block, and or small targets which do not maintain a vertical orientation will not be present in all sections of a TMA
  - Breast ducts and lobules are prime examples

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Problems inherent to tissue: small size of target tissue elements

"Some well-differentiated cancers or other smaller lesions, as well as normal glandular tissues, retained their morphology for a few dozen sections"

Olli Kallioniemi in Tissue microarrays for high-throughput molecular profiling of tumor specimens *Nature Medicine* 7:844, 1998

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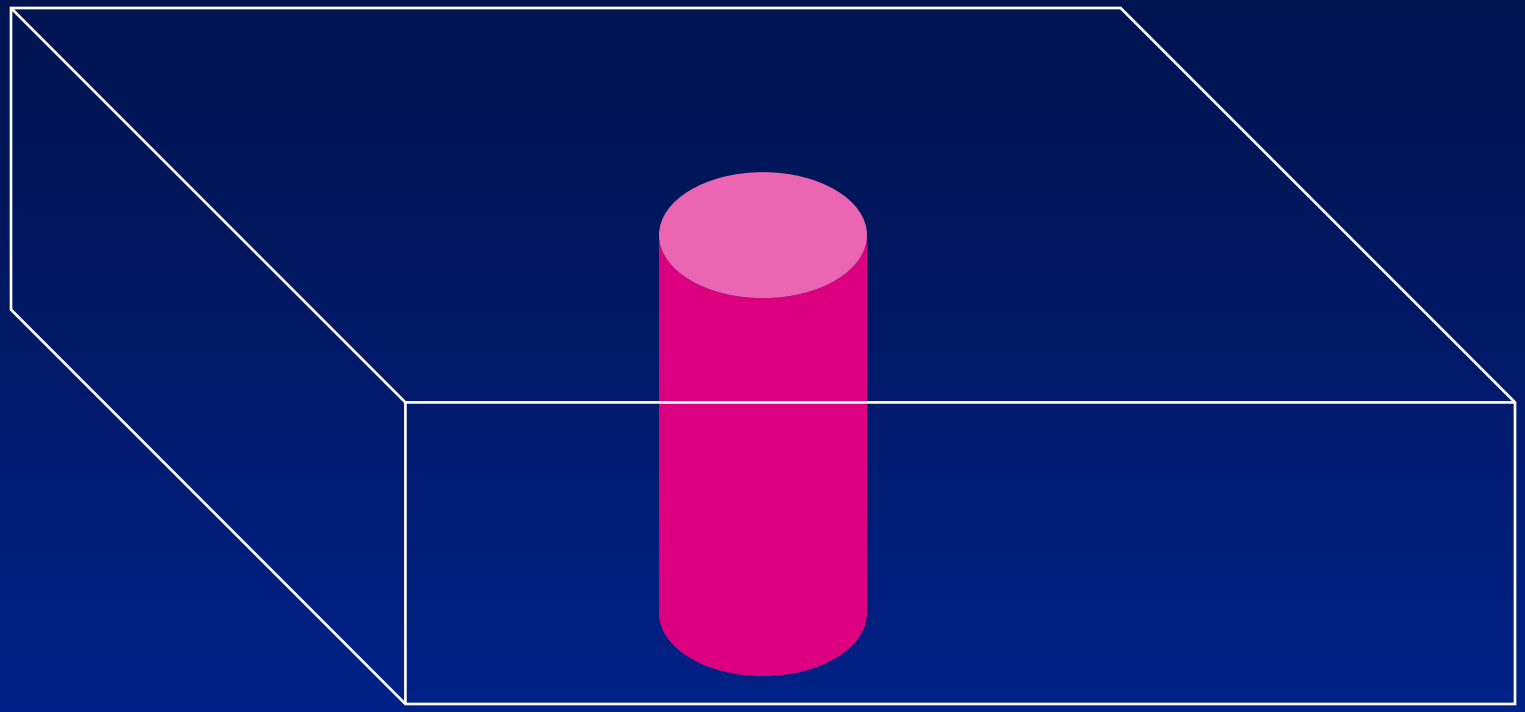

The ideal target tissue architecture is a cylinder, which is the full thickness of the paraffin block.

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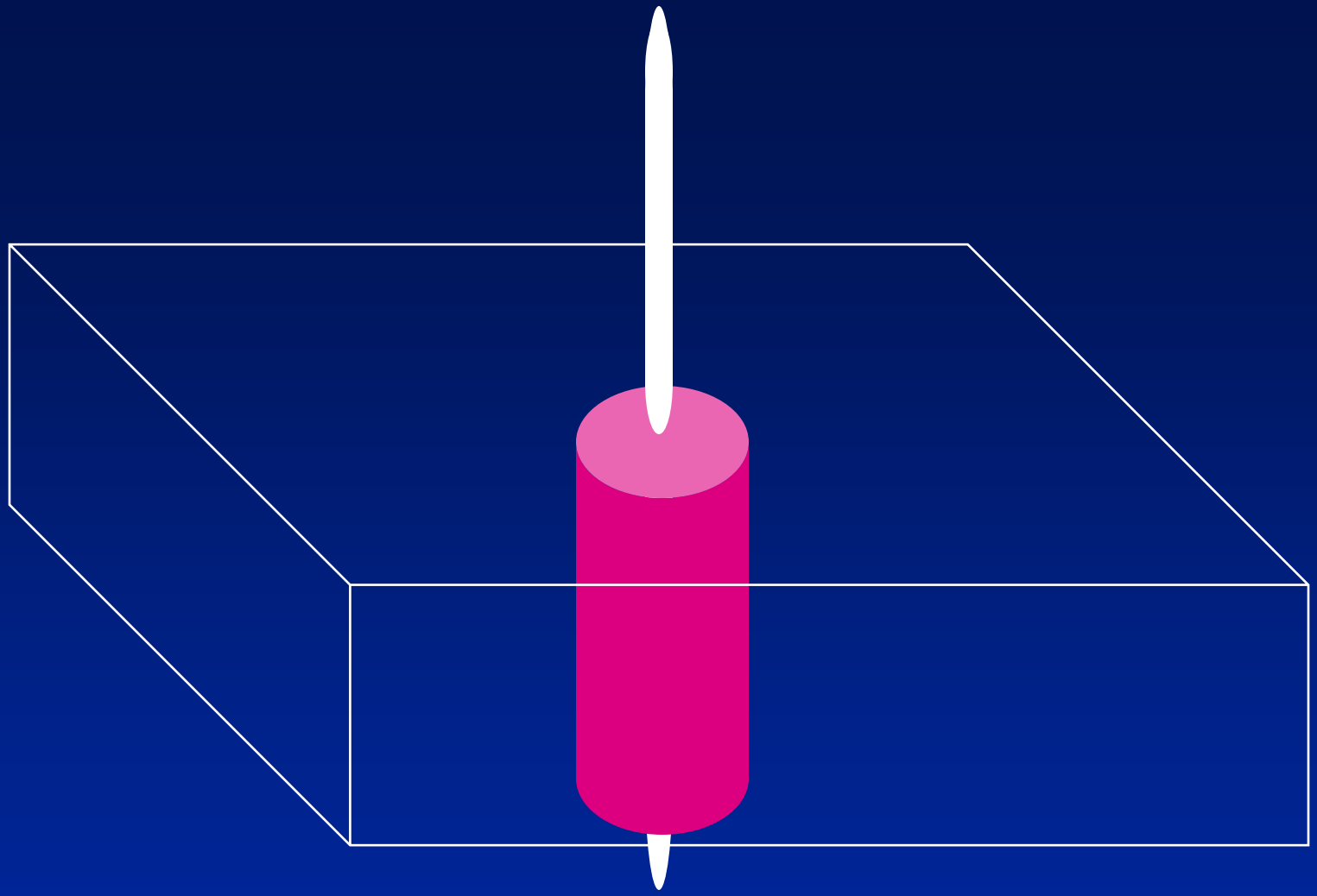

This shape would ensure that target tissue is present in the sampled tissue core in every section of the tissue microarray.

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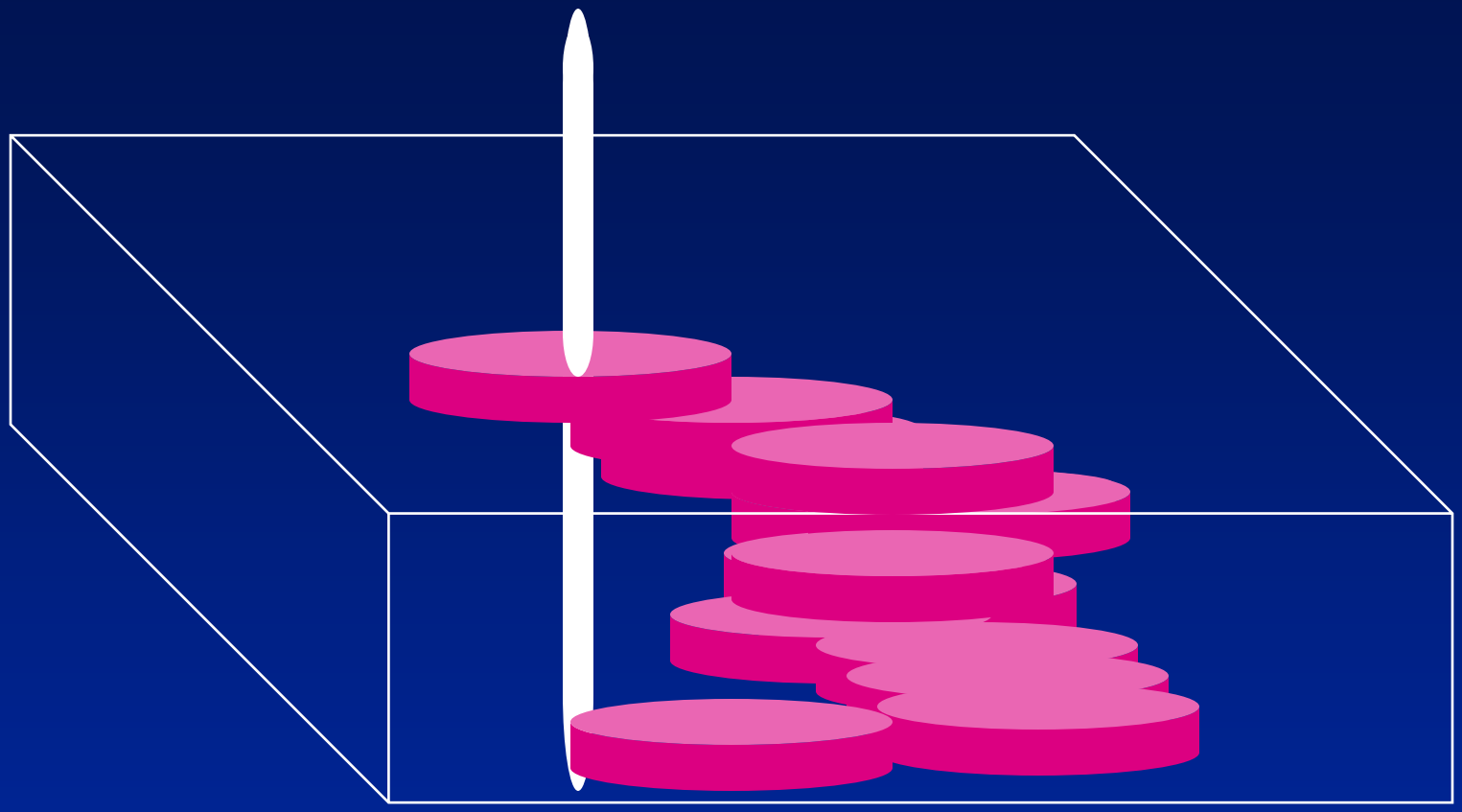

Unfortunately, many tissue elements change their location in the paraffin block and/or are not full thickness. This cannot be fully predicted from examination of the surface of the block.

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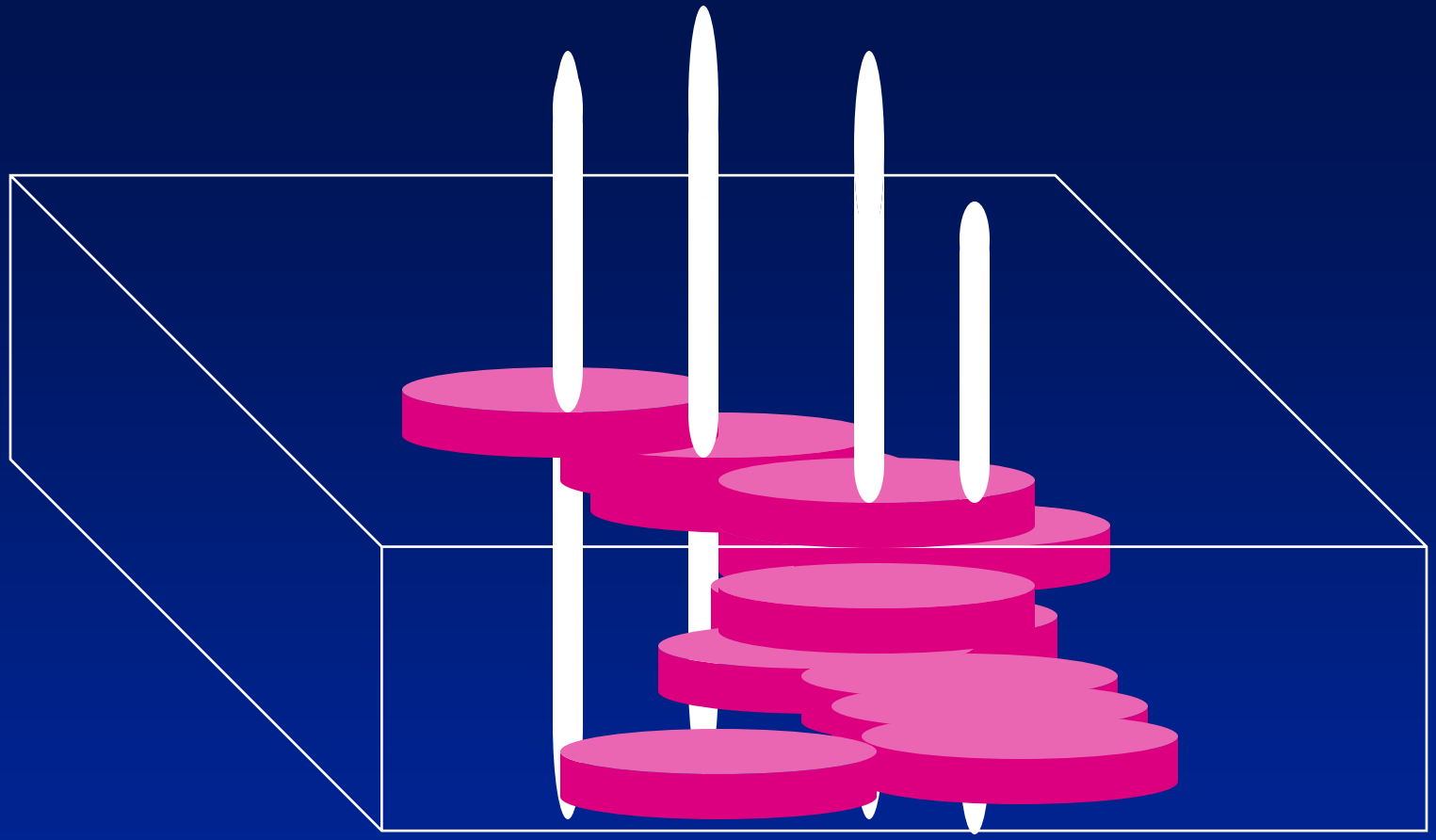

To address this issue, it is wise to consider having more than one core per target tissue in the TMA, and to "double stack" the cores. This helps to ensure target tissue is present in more sections of the TMA.

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Approaches to dealing with "difficult" tissue targets

- Use more than one core to sample tissue
- Use larger core sizes
- "Doublestack" cores

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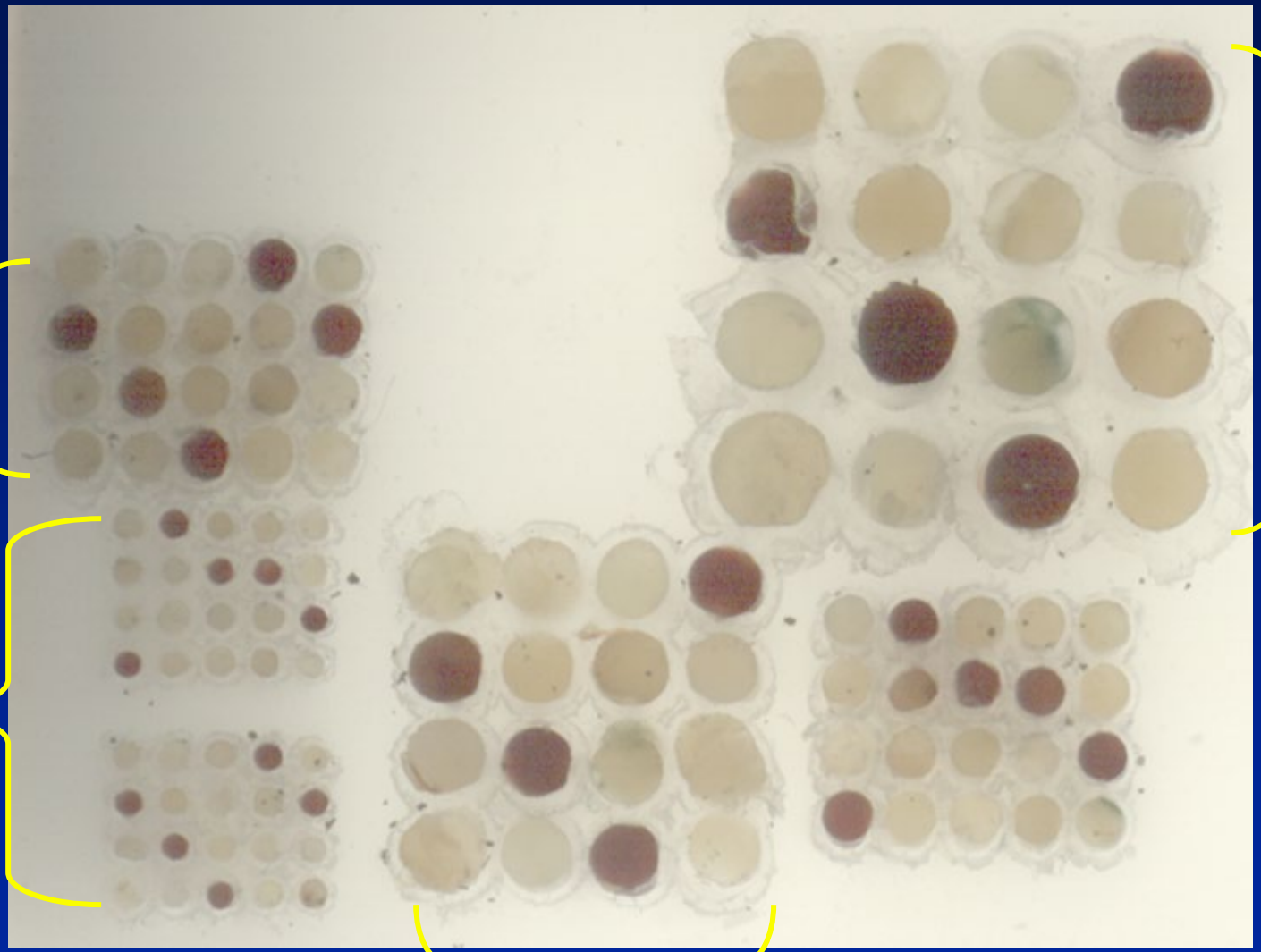
TMA block, with tissue core diameters as indicated



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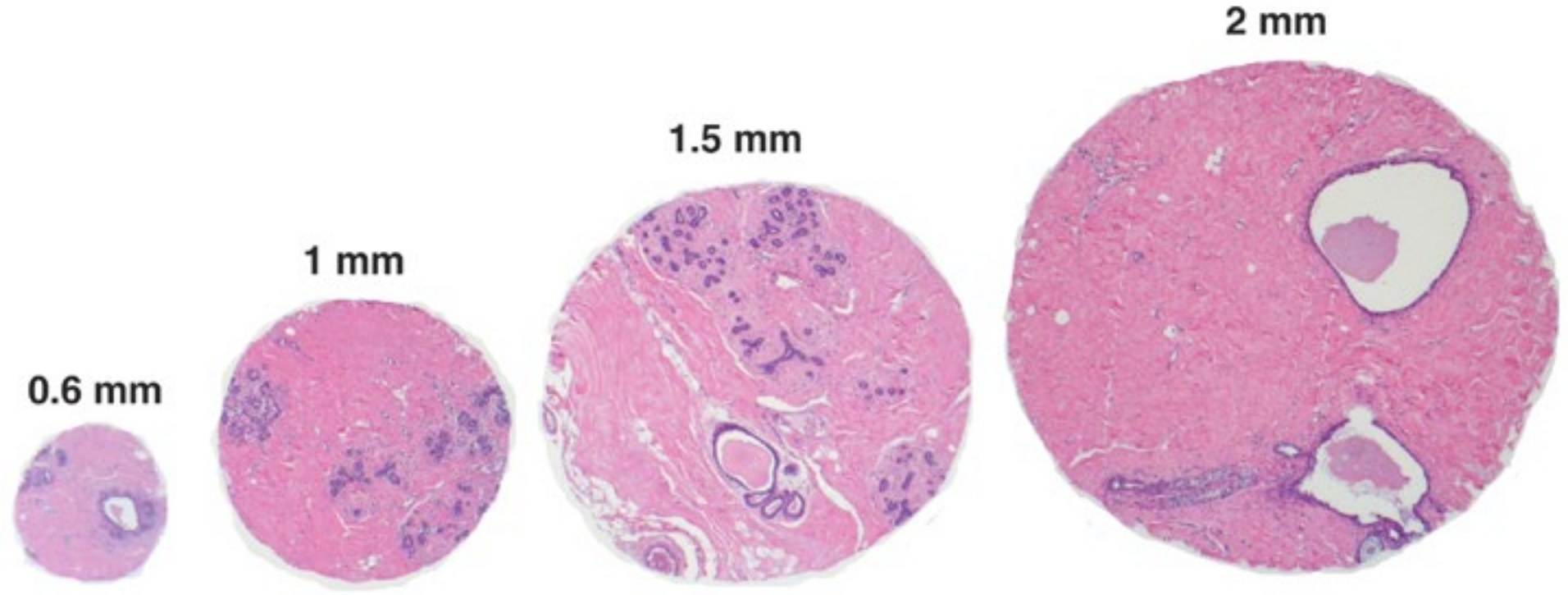
TMA spot sizes: microscopic images



20 X original magnification

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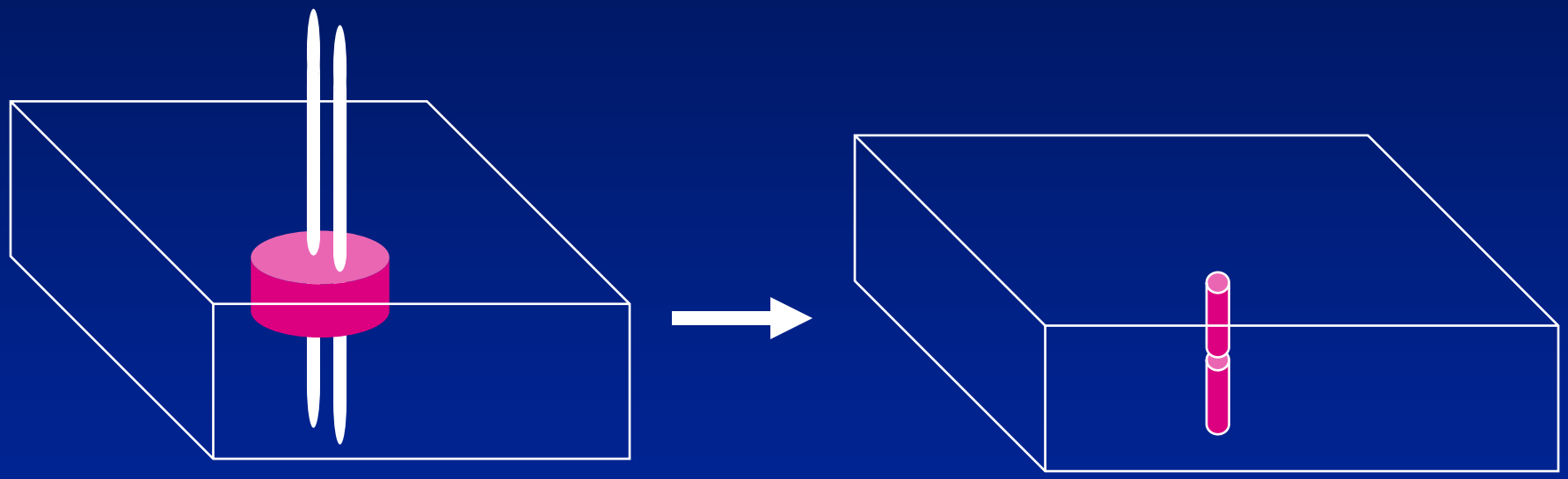
Double stacking of TMA cores



Two cores are removed from target tissue in the donor block.

The cores are stacked, one on top of the other in the recipient TMA block.

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TMA example

- A TMA is to be constructed in 4 copies, with two core positions of target tissue per recipient TMA block, with each core position to be double stacked.
  - Requires 16 donor cores
  - Uses approximately a “square” of donor target tissue with 4 mm sides

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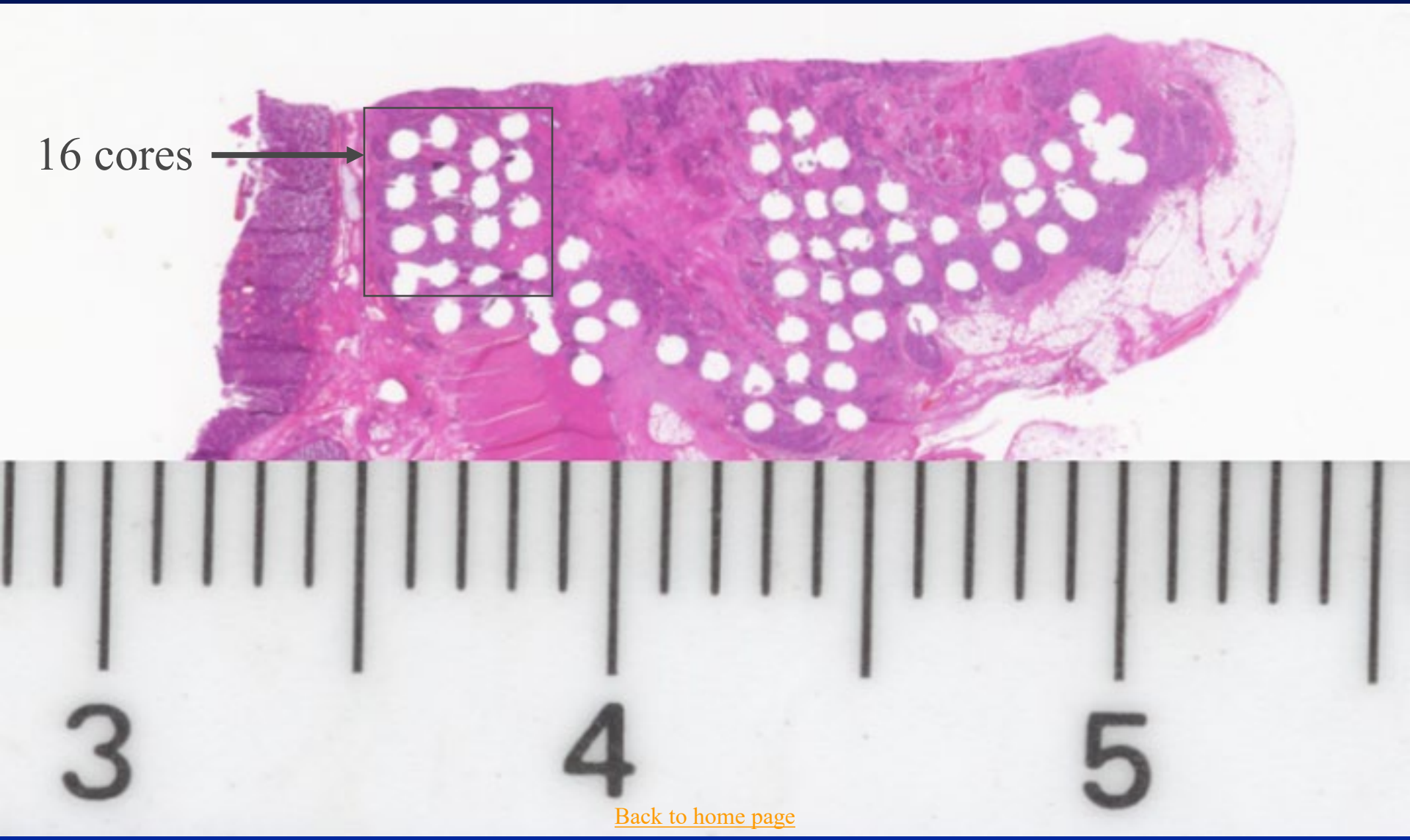
Donor tissue after TMA manufacture



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