Automated whole slide analysis of differently stained and co-registered tissue sections
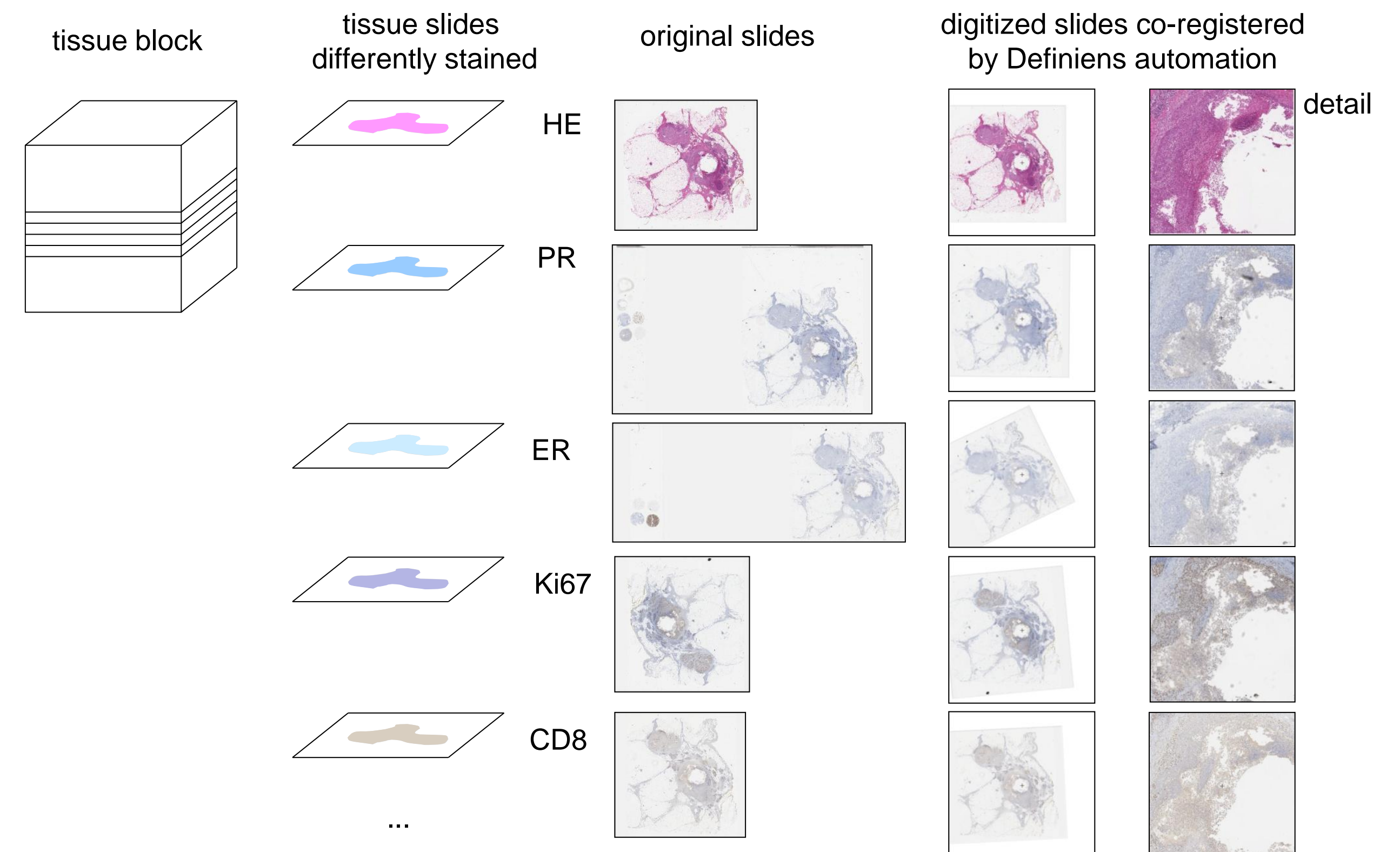
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Abstract

Digital pathology enables applications that are not possible using traditional microscopy and facilitates new ways of handling and presenting whole slide image data, along with quantitative evaluation. Differently stained tissue, highlighting specific biological functions, contains a vast amount of spatial information that must be interpreted by a pathologist. With automated image analysis, some of this information can be quantified and made available for computations such as stain expression analysis. In this contribution we present an automated workflow where quantitative image analysis results of consecutive, differently stained tissue sections are locally fused by co-registration. The results are spatially resolved feature vectors containing features like the densities of positively marked cell types for different stains, which are – in this sense – hyperspectral. Heat maps with many layers (hyperspectral) are generated from this data, revealing relationships between different stains that would not be evident from single stains alone. These hyperspectral data are also a starting point for further investigations; in supporting biomarker discovery in oncology, a systematic search for properties that correlate with clinical data for a patient cohort can be performed in a highly automated way. Together with data mining and machine learning procedures, this constitutes a major component of Definiens' *Tissue Phenomics* initiative.
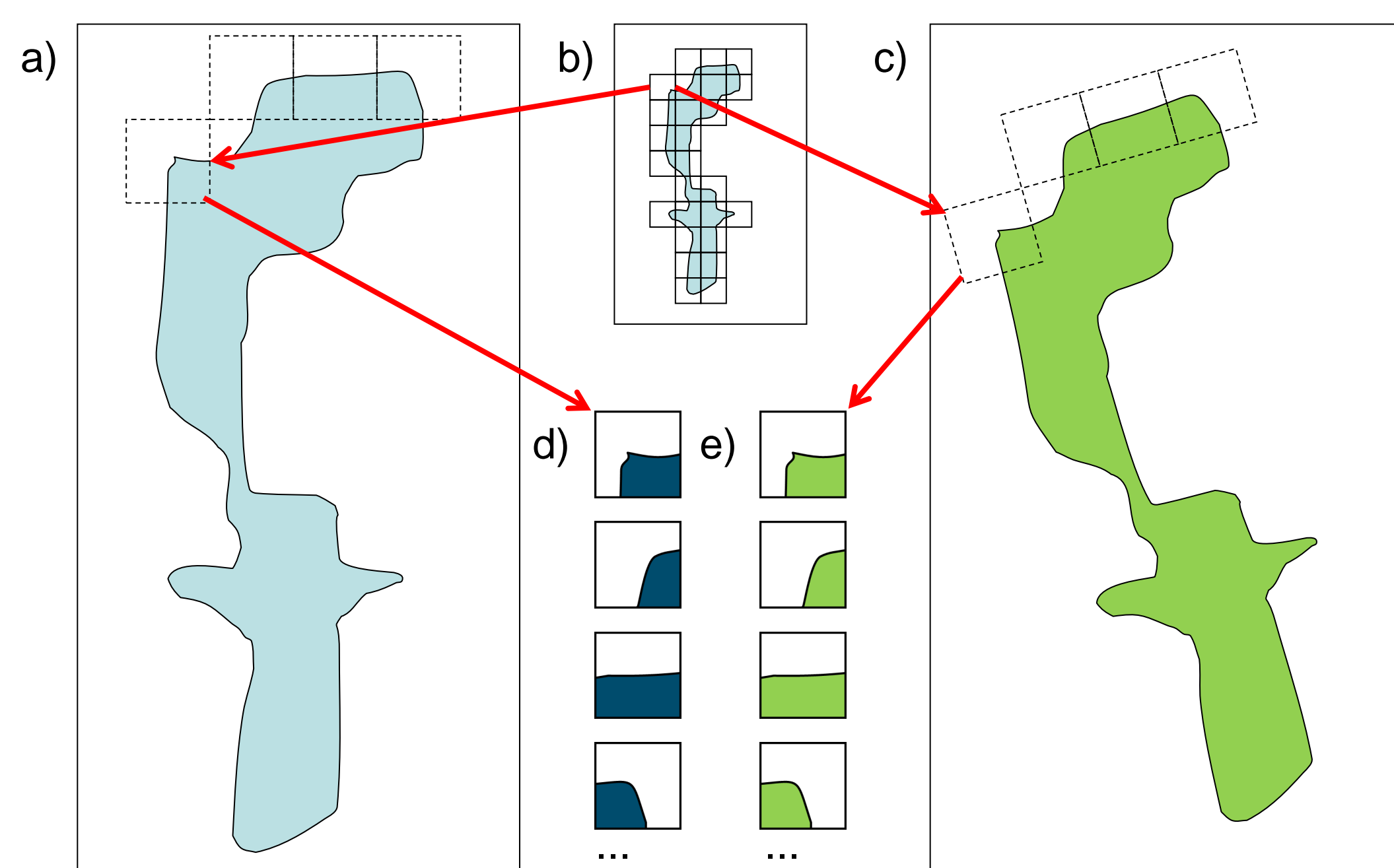
1 Automated image co-registration with Definiens *Cognition Network Technology* to virtually align differently stained tissue sections
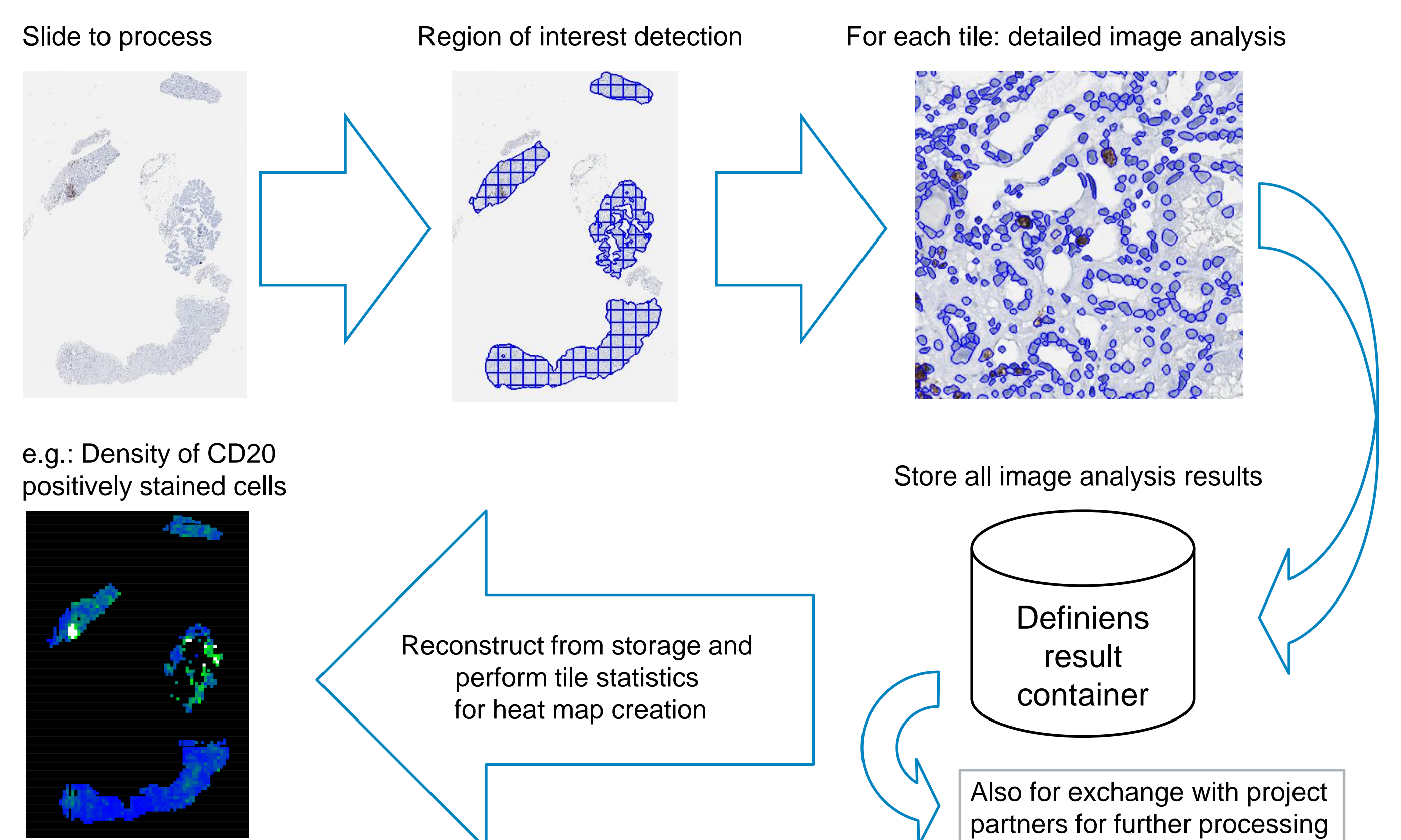

2 Workflow for co-registered tile processing:
(a) master slide, (b) small version of master with tile objects, corresponding regions from (a) and other slide to be co-registered (c) are copied to (d) and (e) at native resolution for detailed image analysis
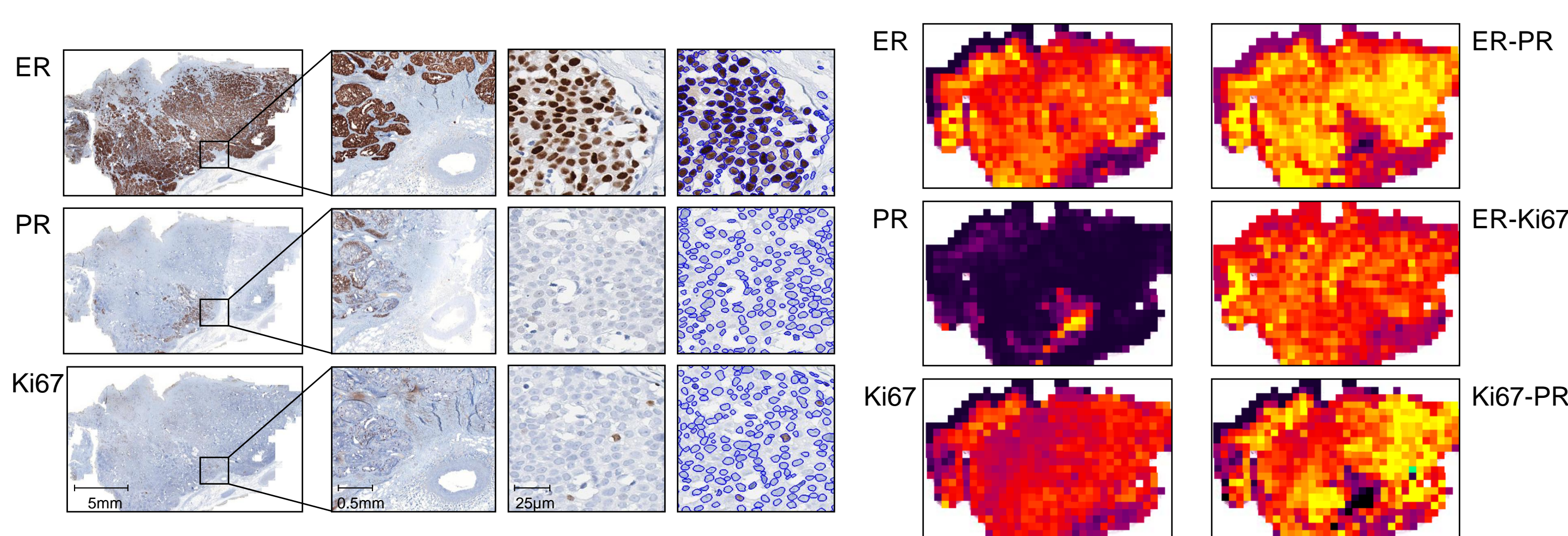

3 Calculation of local statistics for heat map creation

4 Image analysis and *hyper spectral* heat maps:
Slides of different stains are co-registered tile by tile and an automated nuclei detection is performed.
Resulting local statistics for IHC positive nuclei densities is displayed in heat maps. Differences between densities exhibit structures not evident in heat maps of single stains.
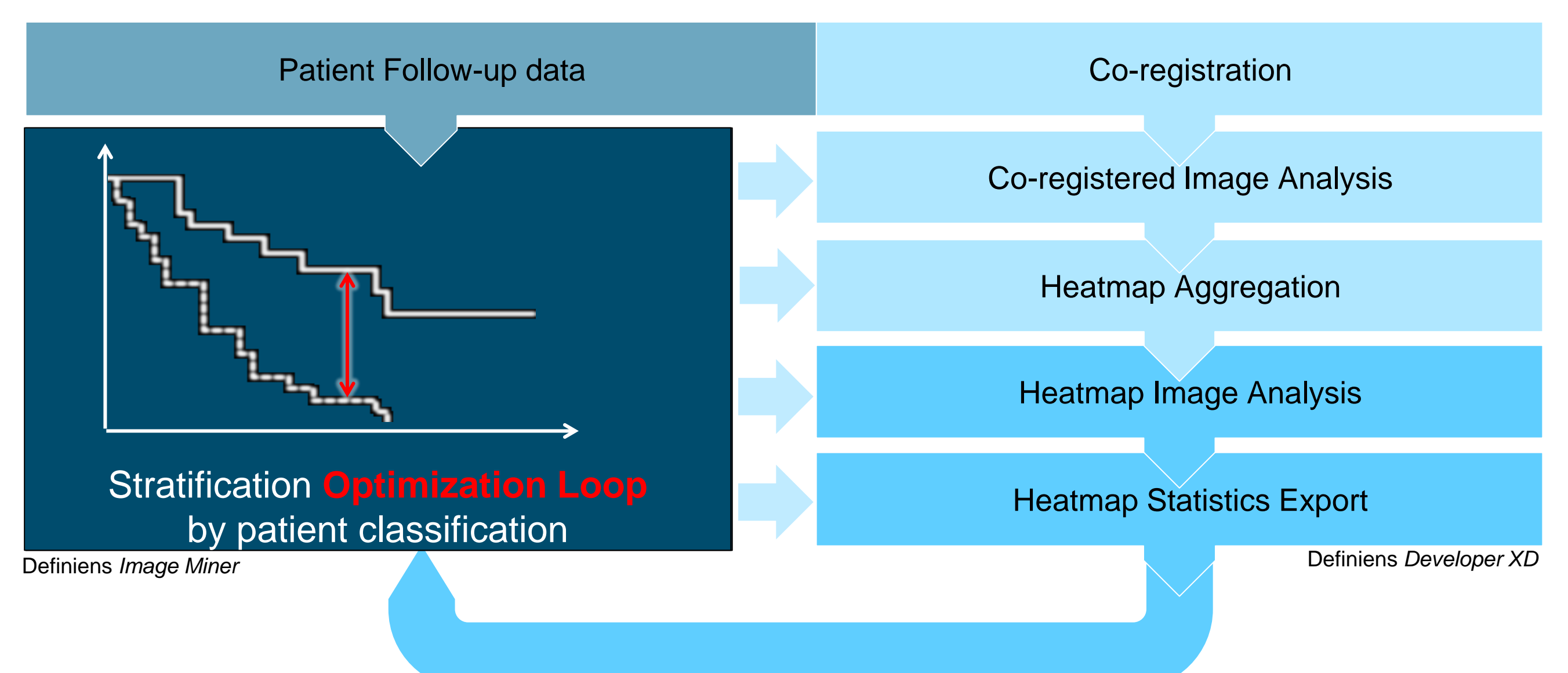

5 Outlook:
Phene Engine delivers tissue-based diagnostic tests

Patient ID	Time of last follow-up after medical intervention started	Patient status at last follow-up	Tissue sections acquired at medical intervention
🧍	📅	1	
🧍	📅	0	
🧍	📅	1	

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