Four tumor micro-environmental niches explain a continuum of inter-patient variation in the macroscopic cellular composition of breast tumors.

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The tumor microenvironment is a complex, self-organising tissue whose architecture determines prognostic and response to therapy. There is significant variation in the cellular and spatial architecture of the tumor-microenvironment within and across patients. Are there rules that constrain the architecture of the tumor-microenvironment? To find out, we develop a quantitative framework of tumor architecture inspired by ideas from satellite imaging, which we apply on deep single-cell profiling and multiplex imaging data in breast tumors. Data analysis shows that inter-patient variation in the macroscopic cellular composition of tumors is structured as a continuum explained by four tumor niches. These niches have their origin in tumor micro-architecture and are shared across patients and tumor subtypes. Niche prevalence depends strongly on the patient, which constraints and explains inter-patient variation. The present framework facilitates interpreting inter-patient variation in terms of a tractable number of micro-environmental niches which serve as organizational entities at the meso-scale to bridge the micro- and macro- scales of tumor architecture.