AI-based "tissue clocks" measure the biological age of human organs

CeMM Research Center for Molecular Medicine of the Austrian Academy of Sciences

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Reviewed

AI-based "tissue clocks" can estimate the biological age of human organs from histological images, researchers at the CeMM Research Center for Molecular Medicine of the Austrian Academy of Sciences and the Ludwig Boltzmann Institute for Network Medicine (LBI-NetMed) at the University of Vienna showed. By analyzing more than 25,000 tissue samples across 40 tissue types, their study reveals that organs age at different rates throughout life and that these changes can even be detected from blood samples. The findings, published in *Nature Medicine* (DOI: 10.1038/s41591-026-04566-5), provide a new framework for understanding aging and may open new avenues for disease monitoring and early diagnosis.

Some people seem to age slower than others, looking and acting like 45 at 60. Others appear to have gotten ahead of the calendar. But why is that, and what is actually happening inside the body? Does a liver age differently from a brain? And is it possible to measure the gap between the age on a passport and the biological age of each organ?

By combining artificial intelligence with one of the world's largest collections of human tissue images, a new study led by CeMM and LBI-NetMed Principal Investigator André Rendeiro and co-first authored by Ernesto Abila, Iva Buljan, and Yimin Zheng, takes a large step towards answering these questions. While previous studies focused mainly on molecular changes such as DNA methylation or gene expression, the team examines how the architecture of tissues themselves changes over time.

A silent diary of time

To do this, the researchers turned to the Genotype-Tissue Expression Project (GTEx), which collected tissue samples from 983 individuals across 40 different tissue types, ranging from the brain and heart to the lung, pancreas, skin, and intestine. These were transformed into high-resolution digital photographs of tissue slices, each revealing the microscopic architecture of the organ in question. The scale is staggering: 25,712 images, representing ~480 million individual image tiles, analyzed with state-of-the-art vision models.

They found that the architecture of organs keeps a silent diary of time: Even without explicitly teaching the AI about it, age turned out to be the single strongest factor shaping tissue appearance across all 40 tissue types. Building on this, the research team developed so-called 'tissue clocks' – predictive models that estimate a person's biological age from the appearance of their tissue, for each organ independently.

These clocks achieved a mean prediction error of just 4.9 years and outperformed existing DNA-based aging estimates in capturing tissue-specific pathology. Importantly, the predicted biological age was strongly linked to known hallmarks of aging, including telomere shortening, tissue pathology, and the number of chronic diseases an individual had.

> *Our tissues carry a remarkably detailed record of the aging process. By combining histology images with artificial intelligence, we can detect patterns of biological aging that are invisible to the human eye and begin to understand how aging unfolds differently across the body."*
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> *André Rendeiro, Principal Investigator at CeMM and corresponding author of the study*

Different schedule for every organ

The analysis revealed that aging does not occur uniformly: Some tissues, such as the lung, kidney, pancreas, and adrenal gland, showed signs of accelerated aging already between the ages of 20 and 40. Others followed more complex trajectories, with peaks of accelerated aging appearing later in life. The uterus displayed a particularly striking shift around the age of menopause. The researchers also identified strong links between tissue-specific aging and medical conditions or lifestyle-associated factors. For example, kidney failure was associated with accelerated aging signals in multiple tissues, while diabetes showed pronounced effects in the pancreas.

"What stands out is how differently each organ ages, and how that shows up in tissue architecture," says Ernesto Abila, co-first author of the study. "Deep learning lets us read these spatial patterns, capturing aging as architectural remodeling, not just molecular drift." While the tissue clocks captured the normal pace of aging across organs, they also highlighted outliers - individuals

whose tissues showed pronounced structural shifts ahead of their chronological age.

However, tissue samples cannot always be collected. By linking blood-based gene expression profiles with the histologically derived tissue age gaps of the same individuals, the researchers built predictors of tissue-specific biological age from blood samples alone. "This is a conceptual leap: using the language of tissue aging, learned from images, and translating it into something readable from a routine blood draw," explains co-first author Iva Buljan.

Blood samples show aging patterns

These blood-based predictors successfully identified aging patterns linked to several diseases, including Alzheimer's disease, Crohn's disease, cystic fibrosis, vasculitis, diabetes, and stroke. In Alzheimer's disease, for example, the strongest aging signal was detected specifically in the brain, whereas Crohn's disease showed accelerated aging across the gastrointestinal tract.

"This study highlights that aging is not simply a matter of chronological time," says Yimin Zheng, the third co-first author of the study. "Different organs age in different ways, and these processes appear to be shaped by both systemic and tissue-specific factors." The findings suggest that tissue architecture integrates many of the molecular and physiological changes associated with aging and disease. In the future, such approaches could contribute to minimally invasive diagnostics that monitor organ health and disease progression through blood tests.

The study also demonstrates the growing potential of artificial intelligence in pathology and aging research. By connecting tissue imaging, gene expression, and clinical data at large scale, the work provides a comprehensive view of how aging manifests throughout the human body.

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