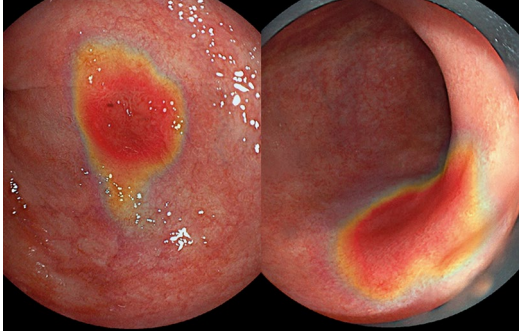


Credit: Two neoplastic lesions showing a heat map visualisation by the CAD system. Adapted with permission from de Groof et al. (2019), Elsevier.

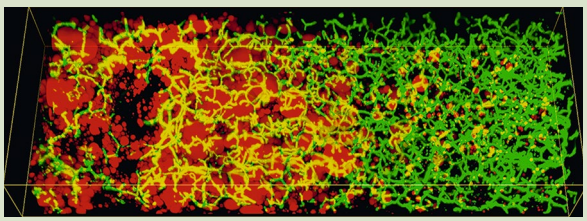
(83% versus 74%). CAD delineations of the area of neoplasm also overlapped with those from the experts in all detected neoplasia.

"This is the first study to externally validate a deep learning CAD system for Barrett neoplasia," concludes de Groof. The group have since conducted, but not yet published, a pilot study using the system in daily practice during live procedures. "Simultaneously, we are developing a video-based CAD system for Barrett neoplasia, that should allow endoscopic detection on video-footage," adds de Groof.

Iain Dickson

> The CAD system outperformed the panel of 53 endoscopists from 4 countries…

ORIGINAL ARTICLE de Groof, A. J. et al. Deep-learning system detects neoplasia in patients with Barrett's esophagus with higher accuracy than endoscopists in a multi-step training and validation study with benchmarking. *Gastroenterology*. https://doi.org/10.1053/j.gastro.2019.11.030 (2019)



3D image of lipid droplets (red) and BC network (green) along the liver lobule of a patient with NAFLD. Image courtesy of H. Morales-Navarrete, MPI-CPG, Germany.

increased pericentral biliary pressure and microcholestasis in steatosis and early NASH that was consistent with increased serum levels of cholestatic biomarkers.

"Due to technical limitations, classical histology overlooks important 3D structures such as the BC," notes Zerial. "Geometrical models of human tissues coupled to computational modelling are a powerful strategy to identify novel biomarkers for early disease diagnosis and to describe human physiology and physiopathology."

Katrina Ray

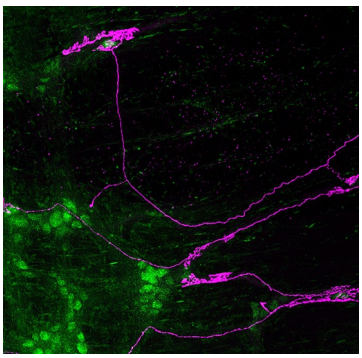
> 3D reconstructions revealed that the BC network was disrupted in NAFLD

ORIGINAL ARTICLE Segovia-Miranda, F. et al. Three-dimensional spatially resolved geometrical and functional models of human liver tissue reveal new aspects of NAFLD progression. *Nat. Med.* **25**, 1885–1893 (2019)

NEUROGASTROENTEROLOGY

Mechanosensing of food in the gut

The regulation of food intake in the gastrointestinal tract is poorly understood. The vagus nerve monitors gastrointestinal signals, and vagal afferents consist of a diverse array of neurons whose sensory endings are specialized for detection of particular stimuli. Now, a new study by Bai et al. uses a single-cell RNA sequencing approach to catalogue the vagal cell types innervating the gut and identify novel roles for intestinal mechanoreceptors and intestinal stretch in food intake regulation.



Top-down view of whole-mount large intestine. Magenta: *tdTomato*$^{+}$ vagal sensory terminals that are labelled using a *Oxtr*^{Cre} mouse line. Green: FluoroGold-labelled enteric neurons. Image courtesy of Z. Knight, University of California, San Francisco, USA.

"First, we developed an atlas that links the molecular identity of vagal sensory neurons to their detailed anatomy," explains Zachary Knight, corresponding author of the study. "This will serve as a resource that allows others in the field to manipulate vagal cell types with high specificity." To do so, the authors injected the fluorescent protein tdTomato into mice, leading to tdTomato expression in vagal sensory neurons. The researchers then catalogued the different vagal afferents and observed several different types of vagal neurons whose unique molecular markers corresponded to distinct sensory endings and innervation patterns. Cell-specific RNA sequencing of vagal sensory neurons enabled the mapping of sensory cell types innervating different regions of the gastrointestinal tract.

Having identified distinct subsets of neurons, the investigators next investigated their role in regulating feeding using mice expressing specific vagal sensory neurons, such as mucosal-ending neurons (*Vip*$^{+}$ and *Gpr65*$^{+}$) and mechanoreceptors with intraganglionic laminar endings (IGLE) (*Oxtr*$^{+}$ and *Glp1R*$^{+}$). "We showed that stimulation of a specific type of vagal neuron corresponding to mechanoreceptors in the intestine can dramatically reduce feeding and inhibit hunger circuits in the brain," says Knight. "This was quite surprising, because intestinal stretch has not traditionally been discussed as a signal that influences feeding." Stimulation of these IGLE vagal mechanoreceptors inhibited feeding, but stimulation of vagal neurons with mucosal endings (chemical) did not. In addition, Agouti-related peptide (AgRP) neurons — a set of hunger-promoting neurons in the hypothalamus (which has a crucial role in the regulation of food intake) that are known to be activated by food deprivation — were rapidly inhibited by stimulation of stomach and intestine IGLE mechanoreceptors but not by nutrient-activated neurons in mice. Moreover, increasing intestinal volume by oral gavage of different fluids inhibited AgRP neurons and food intake, even in the absence of gastrointestinal signals.

Taken together, these findings indicate that intestinal mechanoreceptors and intestinal distension inhibit hypothalamic hunger-promoting AgRP neurons. The researchers hope to further investigate how and when such intestinal mechanoreceptors are naturally activated. "One exciting possibility is that these neurons may be important for the dramatic weight loss induced by bariatric surgery," notes Knight.

Jordan Hindson

ORIGINAL ARTICLE Bai, L. et al. Genetic identification of vagal sensory neurons that control feeding. *Cell* **179**, 1129–1143 (2019)
RELATED ARTICLE Waise, T. M. Z. et al. The metabolic role of vagal afferent innervation. *Nat. Rev. Gastroenterol. Hepatol.* **15**, 625–636 (2018)