PHILIPS

Researchers at Vanderbilt University Institute of Imaging Science unlock the diagnostic potential of sodium MRI

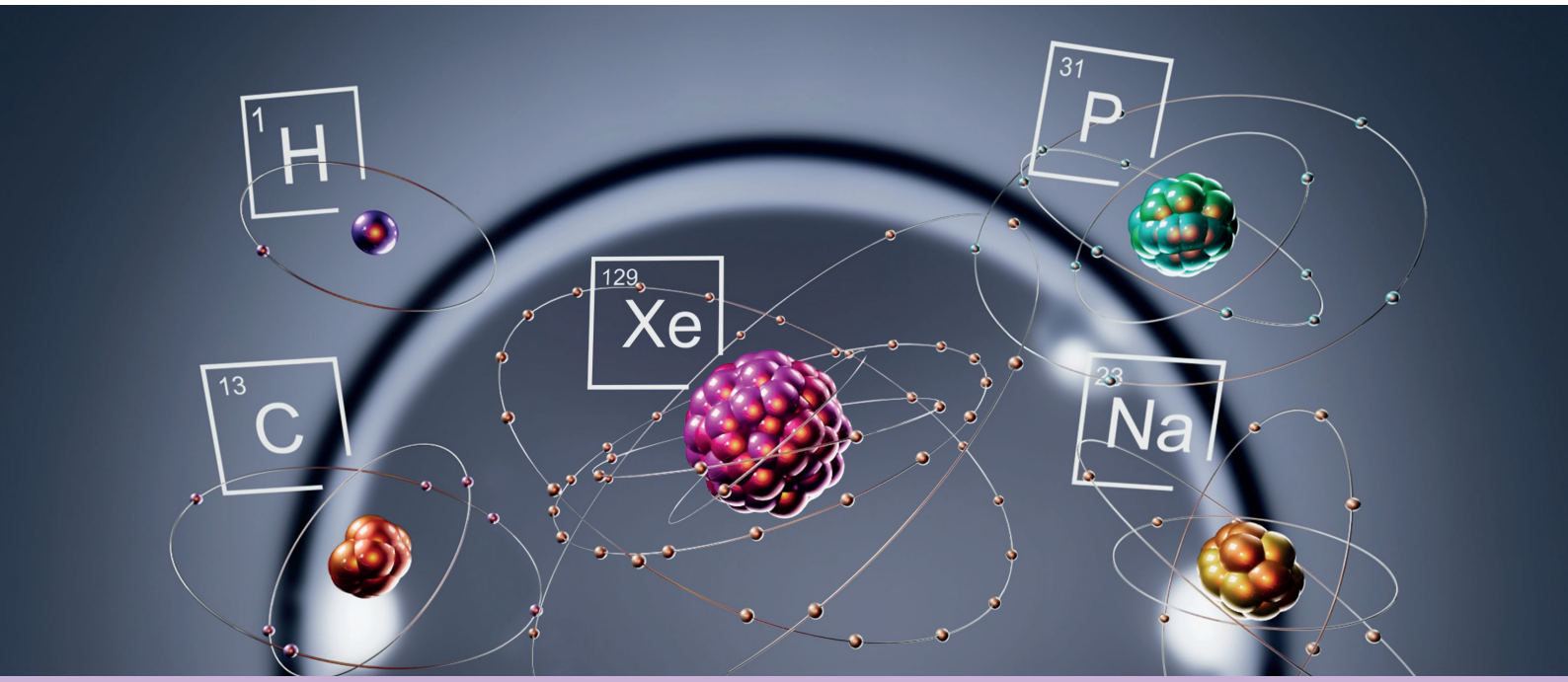
Multinuclear MRI helps Rachelle Crescenzi, PhD at VUIIS in studying lipedema and lymphedema. She found that sodium MRI displays salt retention in the adipose tissue of these patients, which distinguishes their disease from obesity. Her studies aim to support the development of more targeted therapeutic treatments. The ability to combine sodium and proton MRI into one single exam helps develop a fast procedure.

"When patients with lymphatic disease undergo conventional MRI only, the increased sodium in their edema and adipose tissue deposition will stay unnoticed."

Dr. Rachelle Crescenzi,
Vanderbilt University Institute of Imaging Science

Multi-nuclei imaging provides vital information for studying lymphatic disease

At Vanderbilt University Institute of Imaging Science (VUIIS, Nashville, Tennessee, USA), Rachelle Crescenzi, PhD, is using sodium and proton MRI to study lipedema and lymphedema, two medical disorders that are often difficult to distinguish from, or wrongly mistaken for, obesity. She believes the future of research in MRI is related to the imaging of these multiple nuclei. "Not only can we image the structure at the excellent high resolution that MRI provides, but I think really the functional and molecular composition of tissue is where we should be imaging in the future," says Dr. Crescenzi.



Most MRI examinations use signals from protons in water molecules to generate images, because these are the most abundant magnetic nuclei in the body.

However, other magnetic nuclei can be used for MRI as well, including carbon-13, sodium-23, and phosphorus-31.

These substances play different roles in the body, allowing MRI the opportunity to diversify its capabilities with non-invasive exploration of a wide range of biological processes and pathologies beyond the information derived from hydrogen proton imaging. In order to use these molecular imaging capabilities, an MRI scanner needs to have a wide array of sensitivities to the different magnetic nuclei.

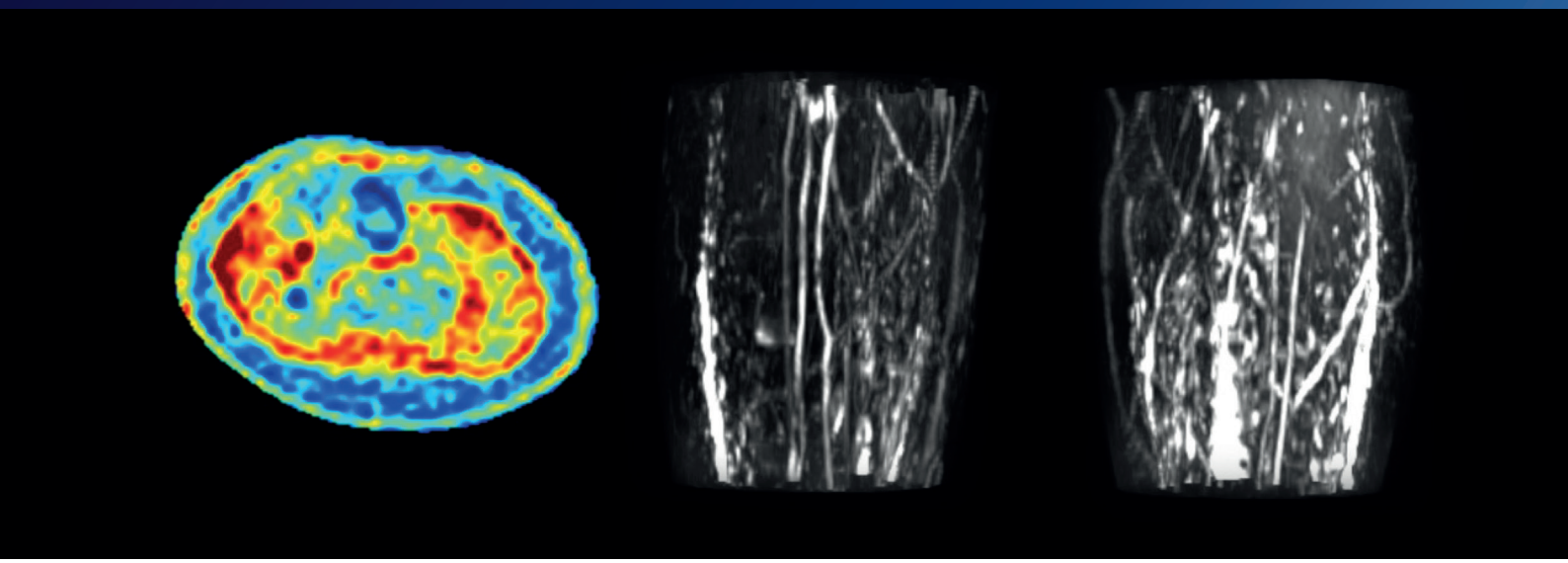
Studies of lipedema and lymphedema in the SALT Lab

Dr. Crescenzi is Assistant Professor Clinical Radiology & Radiological Sciences and Biomedical Engineering. She leads the Sodium, Adipose & Lymphatics Translational Imaging Lab, or "SALT Lab" at VUIIS. Her studies in lipedema and lymphedema started a few years ago with a key observation.

"These patients develop limb swelling which is visible externally as a large volume of their legs or arms, for instance," says Dr. Crescenzi. "But with sodium MRI at 3T, we observe that they not only retain a lot of water, but also a lot of salt. That was an interesting finding and we wanted to follow up on this and understand what salt is doing in the body of patients with lipedema and lymphedema. Could it potentially be a precursor to their later stages of advanced disease?"

"We're interested in applying sodium imaging in long term clinical trials of lipedema and lymphedema to understand the development of advanced disease severity, and if sodium, early in the disease process, could be a marker of risk for lymphatic dysfunction," she says. "Also fascinating are the features of lymphedema with lymph stasis in the body, that we observed with some vascular imaging techniques that we've worked on over the years with our collaborators in radiology and vascular medicine."

Example of standardized tissue sodium content map (left) and example of MR lymphangiography and maximum intensity projection (MIP) reconstruction (right).



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Sodium MRI in studies of upcoming therapies

The SALT Lab's research includes studies of therapies that have been applied to patients with lymphedema and lipedema. A pilot study looked at reductions in tissue sodium following compression therapy. "That was exciting because we learned that therapy could mobilize sodium and that MRI was also sensitive to that sodium mobilization," Dr. Crescenzi says. This was a study performed in collaboration with Dr. Paula Donahue, a certified lymphedema physical therapist at Vanderbilt University Medical Center.

Dr. Crescenzi highlights some exciting therapies that are being developed, such as pharmaceuticals and microvascular surgeries, aiming to clear the lymph and this inflammatory fluid. "We want to follow patients before and after these therapies, so that we can see if there is any connection between improving the patients' lymphatic function and reducing their tissue sodium content. We can measure all of those together with MRI, and we are eager to use these multimodal imaging exams. We hope to make these MRI exams faster, with a comfortable patient scan time, so that we can apply them in longitudinal clinical trials."

"In our ongoing observational clinical trial, we see examples of lymphatic disease every day with our radiologists, as well as limbs of similar size without changes due to lymphatic disease," says Dr. Crescenzi. "When patients with lymphatic disease undergo conventional MRI only, the increased sodium in their edema and adipose tissue deposition will stay unnoticed. In lymphatic disease, it's thought that the adipose results from vascular dysfunction and is different than common adipose due to obesity. Lymphatics disease mechanisms and therapies are still being discovered, and sodium and vascular imaging could play a key part in vital discoveries."

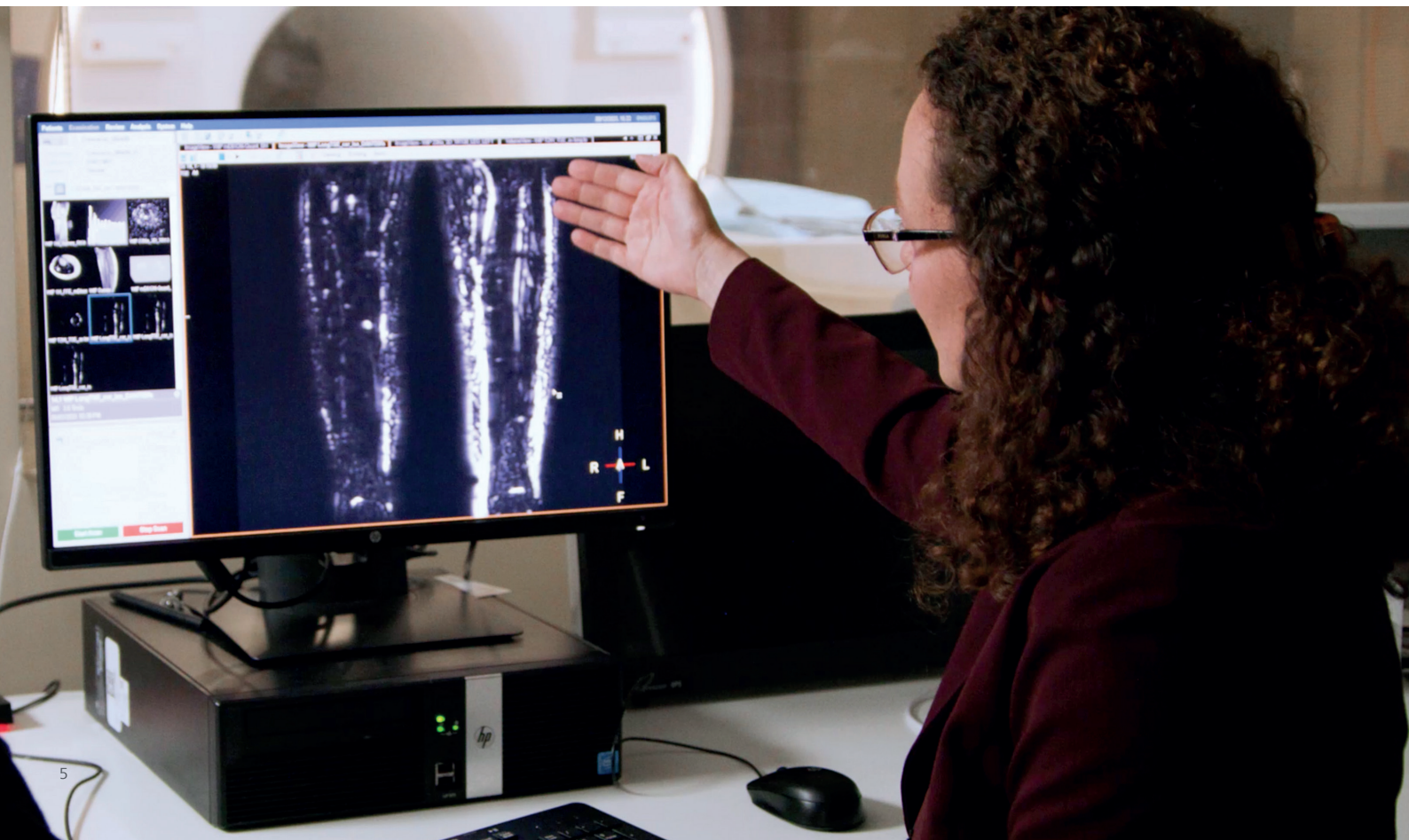
More information is welcomed by radiologists

Dr. Crescenzi notes that radiologists are interested in the additional information that the molecular imaging method can provide, by 3T sodium MRI. "They are hoping that pairing these measures of tissue sodium content with vascular functional imaging, can add new understanding of lymphedema risk factors, and how therapies might modify these."

Although fairly similar to everyday radiology, Dr. Crescenzi's approach for these patients takes it even further. "We are looking at the vascular networks, how they develop, how they change the disease, and how that impacts tissue sodium and tissue fat deposition in diseases like lipedema and lymphedema."

"I don't think that advanced training is needed for radiologists, when they start looking at sodium images," says Dr. Crescenzi. "The standardized protocol allows us to present the sodium signal intensity acquired with MRI in a clinically meaningful metric – millimoles per liter – which radiologists are already familiar with, as it is used for measuring blood sodium concentration.

Very few tools are available to noninvasively measure tissue sodium, and investigators at VUIIS found sodium MRI can help objectively distinguish lymphatic disease from co-morbidities like obesity, which can be highly impactful to patients. "Once these patients have a diagnosis and learn that their adipose deposition is indeed different from obesity, and that it might be related to vascular dysfunction, that opens up a new range of therapies that they may want to choose," says Dr. Crescenzi.



Adding sodium imaging in a proton MRI exam

While common MR imaging is sensitive to the protons of water in the body, imaging of other magnetic nuclei requires different detection hardware, including a radiofrequency coil that is tuned to the resonance of the specific nuclei. Sodium MRI is possible because sodium (23Na) is also magnetic and naturally abundant in the body.

Previously, adding sodium imaging required a separate and time-consuming examination procedure. The current process used in the SALT Lab is much more efficient. “We perform sodium and proton imaging in one series: both protocols are included in a single ExamCard,” says Dr. Crescenzi. “And to overcome the inherently low SNR of sodium MRI, we aim to develop protocols that can sense sodium faster and acquire the scan with higher resolution. These developments, including ultra short echo time (UTE) imaging, are highly relevant to our current clinical trials and to what we think will be important future clinical developments.”

Multi-nuclear MRI ExamCard and review.

"We perform sodium imaging in series with other vascular and anatomical MRI scanning – it can be done in the same ExamCard and runs just like any other lower extremity scan."

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Sodium and proton MRI in one examination

Performing leg sodium MRI starts with the technologist positioning the patient feet-first into the 3-tesla magnet. "No specialized training is required – a technologist who can run other lower extremity MRI exams is perfectly capable of running the multi-nuclei exam," says Dr. Crescenzi. "In fact, we perform sodium imaging in series with other vascular and anatomical MRI scanning: it can be done in the same ExamCard and is run just like any other lower extremity scan."

Sodium MR imaging in the lower extremities is performed first, using a dedicated sodium coil. "We use multi-nuclei MR spectroscopy and imaging to perform sodium MRI in series with other scans like mDIXON MRI and MR lymphangiography," says Dr. Crescenzi. "Once the sodium MRI is acquired, the subsequent scans can acquire proton imaging just like any other ExamCard. And all of this can be performed by the MRI technologists."

"Our MRI technologists all learned the standardized sodium protocol, which is used in multiple clinical trials at the imaging institute. We have optimized and modified the ExamCard parameters with our imaging trainees and translated this back to the technologists who operate the scanner day in and day out. Integration of sodium and proton MRI capabilities has increased our scan time efficiency which aims to improve the adoption of noninvasive molecular imaging by sodium MRI."

Multi-nuclei MRI poised for broader application

According to Dr. Crescenzi, it is not only the small niche of lymphatic diseases where sodium imaging could have an impact. There are also renal, cardiovascular and metabolic diseases that affect sodium in the body.

Pediatric vascular medicine specialists currently have very few technologies for differentiating a venous from a lymphatic malformation. "The ability to perform MR lymphangiography with the capabilities now available on our three-tesla clinical scanners is very attractive to the radiologists and the vascular medicine specialists in the hospital here," says Dr. Crescenzi. "I believe that if we had sodium MRI on top of vascular functional imaging in the hospital setting, it could really transform how some rare vascular diseases are being treated and diagnosed in the clinic. Being able to perform multi-nuclei imaging at clinical field strength 3T will be critical to getting these technologies into the hospital."

Dr. Crescenzi appreciates the collaboration with the vendor and their onsite clinical scientist. They worked jointly on improving technologies for proton imaging and multi-nuclei sodium imaging, and are driving standardization of sodium imaging technology across different sites in the network.

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Patient needs are what motivates researchers

According to Dr. Crescenzi, hearing from patients about their most troublesome symptoms is what really motivates her team's research. "These patients are often told that they have common obesity, when they actually have something very different from obesity, that involves together sodium, adipose and lymphatics. We want to develop sodium imaging together with MR lymphangiography in a short, clinically feasible scan time."

"I think that finding a cure for lymphatic diseases is a real possibility. Consider how treatment development has often started with better technologies to evaluate therapies in clinical trials. We want to make the sodium imaging faster and acquire higher resolution images to better test the impact of therapies on lymphatic disease and monitor long term outcomes," she concludes.

Summary

- The SALT Lab uses sodium MRI and proton MRI to study lipedema and lymphedema, that are often difficult to distinguish from obesity.
- In clinical trials, sodium MRI shows salt retention in patients with lipedema and lymphedema and allows measurement of tissue sodium noninvasively.
- Radiologists are interested in the additional information that sodium MRI provides when pairing it with vascular functional imaging.
- Sodium MRI can be seamlessly integrated in a series with other vascular and anatomical MRI scans, all in the same ExamCard.

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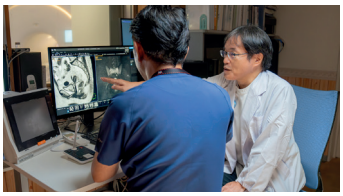

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