Digital autopsy

A new contrast injector and a high-power MRI help to ascertain causes of death

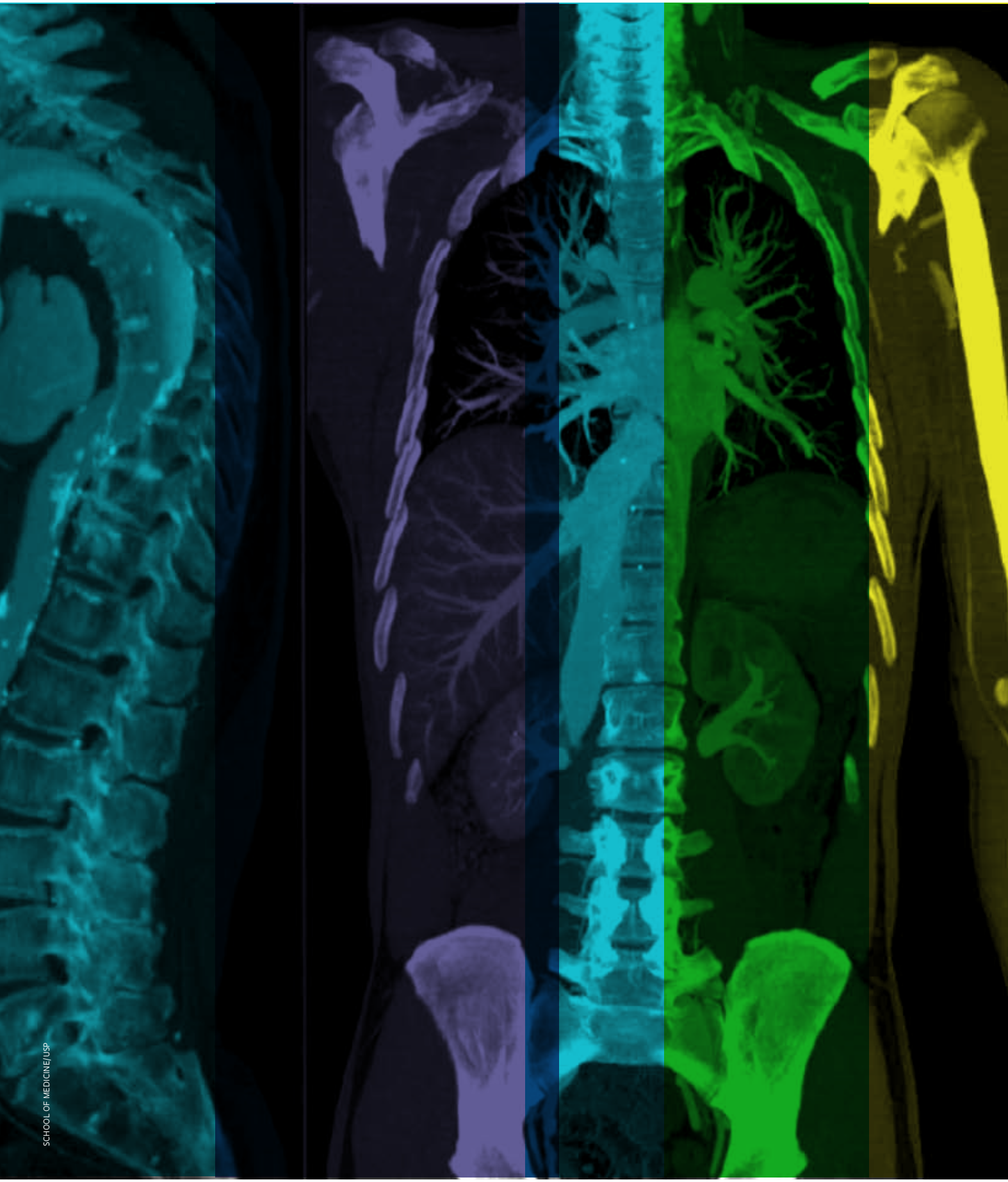
Marcos de Oliveira

PUBLISHED IN JUNE 2013

The most celebrated portrayal of a human dissection is a 1632 oil painting by the Dutch artist Rembrandt. Known as *The Anatomy Lesson of Dr. Nicolaes Tulp*, the picture shows seven earnest medical students looking at the body of a criminal stretched out on a table, with one of his arms sliced open and the inside exposed. Over the centuries, medicine has relied on the type of procedure that Rembrandt depicted not only as part of medical training—so that future doctors could learn about the workings of the human body and its diseases—but also as a means of determining cause of death when necessary. The current trend worldwide is to use standard medical equipment such as CT scans and MRIs to "see" the cause of death without needing to cut open the body of the deceased. However, the scientific foundations of these approaches are still limited. One of the most ambitious studies in this realm is being conducted in São Paulo at the University of São Paulo School of Medicine (FMUSP). There, under the coordination of Prof. Paulo Saldiva, head of the Department of Pathology, a group of researchers is testing ways to conduct an autopsy using images obtained using tomography equipment. Working in conjunction with the company Braile Biomédica, located in São José do Rio Preto, state of São Paulo, the group has developed an injection pump that introduces contrast through an artery in the groin of a corpse; from there, the agent spreads through the body, producing high-quality images.

The researchers expect to take a large step forward in their studies in 2014, following delivery of a high-field magnetic resonance scanner — the first in the Southern Hemisphere — purchased with funds totaling US$7 million from three sources: FAPESP, the São Paulo State Department of Health, and USP. "As medicine has evolved and as methods have been adopted from biochemistry and cell and molecular biology, along with imaging techniques, autopsies have become a thing of the past, even in the specialization of doctors," says Saldiva.

Full-body colored CT images of cadavers



SCHOOL OF MEDICINE/USP

"Autopsies are a lot of work; they can take up to three days to do, and they pay poorly." He reports that medical autopsies have decreased worldwide in the case of death by natural causes. The situation is different in forensic medicine, which addresses violent deaths, such as those resulting from gunshots and stabbings. In these cases, a body must be processed at the Instituto Médico Legal (IML), where a forensic physician, who generally has police academy training as well as a degree in medicine, prepares reports for criminal investigations and legal processes. "Medical autopsies are for cases where people are found dead at home or in a public place, or who arrive at an emergency department DOA, for example, and the doctors don't know what cause to put on the death certificate," Saldiva explains.

These ambitious studies on digital autopsies are made possible by new equipment at the School of Medicine. They are important because USP is responsible for the Death Certification Service of the city of São Paulo (Svoc), which has been attached to the university since its creation by a state-level decree in 1939. The service processes all cases in the municipality of São Paulo that require medical autopsies. "This is the largest medical autopsy service in the world," Saldiva said. "No other has ties to a university; the Svoc is an agency like the Paulista Museum or the Institute of Tropical Medicine, attached to USP. Anyone who dies in São Paulo and doesn't have a death certificate is brought here." More than 13,000 autopsies a year are performed at the Svoc, and many studies are conducted there as well, always with the approval of family members. Unclaimed bodies—for example, of indigents—are not autopsied. In 2012, there were 194 such cases. "We have all of these autopsies on hand, and with them we can further our research and develop new knowledge, in addition to relying on the collaboration of all departments in the School of Medicine. Today there are questions about the role of the autopsy as a source of scientific knowledge. We want to prove that an autopsy can be extremely useful when it incorporates new technology," Saldiva says.

"We want to prove with these images that an autopsy can still be extremely useful and can offer new knowledge," says Saldiva

1 Three-dimensional reconstruction based on a CT scan. Organs are shown in red. Bones and the contrast inside blood vessels are shown in white to gray tones

2 Images of the heart

DISCOVERING DISCREPANCIES

In a scientific article published in the journal *The Lancet* in 2012, a group of researchers from Oxford University presented a study that analyzed 182 deaths, using CT scanning and MRIs alone, without any biopsies. "With the support of the Svoc, we are able to perform 1,000 autopsies a year using images and biopsies," Saldiva explain. "We can do a minimally invasive autopsy and a conventional autopsy on the same body. We believe a minimally invasive autopsy is better than the conventional in some situations but not in others. We will be able to define these cases and figure out where the new technique works and where it doesn't."

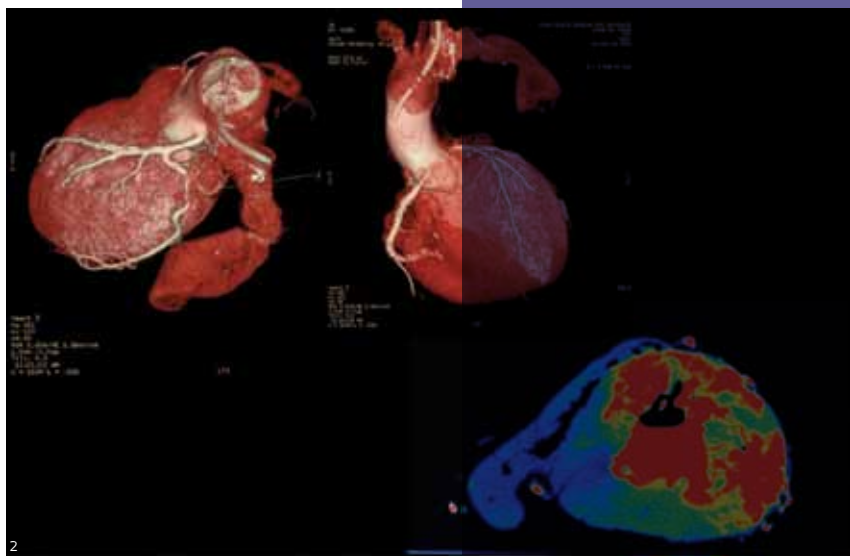
The scientific bases for using imaging studies have been established only in the case of violent death. Post-mortem imaging was developed in the sphere of legal medicine, with Switzerland leading the way. "You can see lesions, bruising, fractures, and where the bullet entered and what its trajectory was, without

cutting open the body and then displaying the images before a judge and jury," Saldiva says.

A medical autopsy, according to Saldiva, first serves to determine a person's primary cause of death. It is then possible to identify an underlying illness that may have contributed to the death. It is also possible to ascertain whether any treatment that had been given was appropriate and if there were any complications stemming from it. "There's room here for quality control at hospitals," he says. Saldiva remembers a study conducted at Massachusetts General Hospital, which performed a comparative analysis of autopsy results over a 30-year period and found that serious mistakes had been made in 10% of cases, mistakes that would have altered the stated cause of death. "At the hospital connected to Harvard University, 11% of the autopsies presented errors, while a rate of 15% was found at Hospital das Clínicas in São Paulo. Of course, there is a bias towards selecting more complicated cases for autopsy, and this might lead to the discovery of more mistakes than usual," he says.

"From a research perspective," Saldiva adds, "autopsies have an unimaginable contribution to make. When it comes to analyzing brains in the case of age-related diseases such as Alzheimer's, they're an extremely important tool because there's no way you can do a biopsy on a living person." He believes that MRIs and other new imaging tools will help in the selection and analysis of brain tissue for the brain bank now being assembled at USP. However, he wants to go further by identifying and correlating deaths in each region of the city of São Paulo. "If there's a concentration of young women with breast cancer in a certain region of the city, we can detect it. It's a way of assessing the relationship between genome and environment," he says. He dreams of collecting the data on the 13,000 autopsies performed at the Svoc annually and studying each person's habits—for example, determining their diet—and then mapping out diseases, especially those linked to air pollution.

In practical terms, the quality of research at the School of Medicine has been enhanced by the injection pump, which introduces contrast composed of iodine and polyethylene glycol, a viscous solution. "We'd been told about a device in Switzerland that cost €100,000, but the contrast was very expensive and would have to be imported. So we spoke to Domingo Braile [a surgeon and one of the owners of Braile Biomédica; see *Pesquisa FAPESP* Issue No. 176], and he offered us access to his team," says Saldiva. "We adapted the heart-lung machine that we use in cardiac or lung surgery so that it can inject the contrast. We added some controls, especially in relation to the flow of the liquid, which has to be well monitored so that no blood vessel is accidentally ruptured," says Marcos Vinicius, an electronic engineer and the superintendent of testing at Braile.



2

The injection pump developed by Braile will work with the new MRI equipment

SPECIAL SHIELDING

The injected contrast not only yields better images but also makes it apparent whether a vein or artery has broken open. "The equipment is very capable and flexible in developing the functionalities that our projects demand," says Prof. Luiz Fernando Ferraz da Silva, a member of Saldiva's group. Brazilian technology offers another advantage: the design of software tailored specifically to this research. Together, the company and USP are analyzing the possibility of applying for a patent on the equipment, which should ultimately cost US$ 43,800 – US$ 65,600.

The injection pump is also being designed to work with the MRI machine that will be installed in a suite of rooms on the lower level of the School of Medicine. Oversight of the installation of the rooms and equipment is in the hands of Prof. Silva, who explains that heavy shielding around the room — made from 400 metric tons of iron — is needed to contain the emissions from the strong magnetic field. Without this shielding, people who have metal prostheses or pacemakers could have problems if they were too close to the equipment. The MRI has a magnetic field of 7 teslas (T). "Clinical machines, like those used in hospitals, for example, have 3 teslas," Silva notes. "We were going to purchase a 3-T, but at the request of the staff in radiology, we bought one that is more appropriate for research purposes," says Saldiva. "Only Germany, the United States, England, Japan, Switzerland, and France have this type of MRI, which has not been approved for use in clinical tests yet."

Project

Image platform in the autopsy room (No. 2009/54323-0); **Grant Mechanism** Multi-user Equipment Program (EMU); **Coordinator** Paulo Hilário Nascimento Saldiva - USP; **Investment** R$3,000,000.00 (FAPESP), R$3,000,000.00 (USP), R$1,500,000.00 (School of Medicine Foundation), and R$3,000,000.00 (USP).

IMAGES SCHOOL OF MEDICINE/USP