

Pathology's Role in Liver Transplantation Surgery: Offering Patients a New Lease on Life



Montefiore recently became the first health system in New York City to perform a liver transplant using a donor liver infected with the hepatitis C virus. The first Montefiore patient to undergo the procedure was a 21-year-old man with multiple autoimmune disorders. Because of a chronic donor-organ shortage in New York State the gravely ill patient had been waiting 14 months for a new liver. So, when the hep C-positive organ became available, he and **Samuel Sigal, MD**, his hepatologist, came to a decision: replacing his own irreparably damaged liver with an infected one that could be treated was his best chance at survival. Earlier this month, the case landed on the cover of [Crain's New York Business](#).

An average of 50 liver transplants are performed each year at Montefiore under the direction of **Milan Kinkhabwala, MD**, chief of transplantation and the director of abdominal transplantation at the Montefiore Einstein Center for Transplantation.

“Montefiore’s anatomic and surgical pathologists are integral members of our liver transplantation team,” says Dr. Kinkhabwala.

The Montefiore Einstein Pathology Department's Surgical Pathology Division includes four anatomic pathologists who specialize in liver disease and transplantation: **Kathryn Tanaka, MD; Qiang Liu, MD; Nicole Panarelli, MD; and Sun Chung, MD.** Drs. Liu, Panarelli and Chung participated in the transplant described above, performing a pre-operative bile duct biopsy, an explant liver analysis and a post-transplant liver biopsy.

Background

Liver disease is one of the leading causes of death in the United States. For patients with severe liver disease, a life-saving liver transplant may be warranted. According to the American Liver Foundation, about 6,000 liver transplants are performed in the U.S. each year and the number is on the rise.

The Bronx has one of the highest rates of liver disease in the nation and the highest prevalence in New York State. Diabetes and obesity, two risk factors for developing liver disease, have reached epidemic levels in the New York metropolitan area and nationally. Both are major health problems in the Bronx.

In 2008, to address the growing need, Montefiore established the Montefiore Einstein Center for Transplantation, the first and only facility of its kind in the Bronx and one of the four leading transplantation centers in New York City.

When is a Transplant Indicated?

Cirrhosis -- a chronic condition caused by fibrosis (scar tissue) -- is the most common reason for liver failure leading to the need for a transplant. The most common cause of cirrhosis in the U.S. is the hepatitis C virus.

Alcohol abuse, non-alcoholic fatty liver disease, non-alcoholic steatohepatitis, autoimmune liver disease and liver cancer can also lead to cirrhosis.

A less common condition for which a transplant may be indicated is acute liver failure, which can occur in patients with no previous history of liver problems.

The Anatomic and Surgical Pathologist's Role



Dr. Qiang Liu, surgical pathologist, examines a liver tissue sample. Dr. Liu arranged for three liver transplant surgeons from China – where organ transplantation is relatively new – to visit Montefiore for a month in spring 2017 to observe liver and other organ transplant procedures.

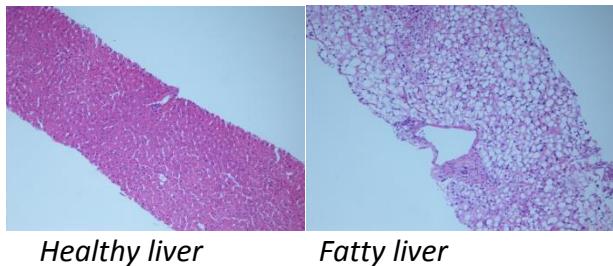
Pathology plays a vital role in liver and other organ transplant surgeries, both before and after surgery.

The transplant surgeon relies on the pathologist to:

- help make the initial diagnosis to determine if a transplant is indicated;
- assess whether the patient is a good candidate for transplant;
- determine if the donated organ is healthy;
- help identify post-transplant complications such as rejection of the transplanted organ;
- review the diseased liver (explant pathology) to assess the accuracy of the initial diagnosis so that an appropriate post-operative treatment plan can be implemented.

Pre-operative Procedures

Patients in need of a liver transplant receive a MELD (Model for End-State Liver Disease) score based on the severity of their condition, and are placed on a waiting list. When a potential organ donor dies, a needle biopsy is performed on the cadaver liver or a biopsy is performed on a living organ donor. As is often needed, the pathologist does a frozen section to rapidly analyze the tissue sample and determine whether the organ is healthy.



Montefiore belongs to a network of hospitals on the East Coast. When a donor liver is identified at Montefiore, the surgeon performs a biopsy. If the liver is healthy, it's sent to the hospital where the designated recipient is located. (The donor organ must be delivered within 12 hours to remain viable.)

Conversely, if the recipient is a Montefiore patient, Montefiore surgical fellows travel to the site and harvest the donor liver. The Montefiore Einstein (or other hospital) transplantation program's Immunology Laboratory determines if there is a match between the donor liver and the potential recipient.

The Surgical Pathology team is on call 24/7, ready to spring into action whenever an urgent liver biopsy is needed.

Post-operative Protocols

After transplant surgery, the patient is prescribed immunosuppressive drugs to prevent the body from attacking the transplanted liver.

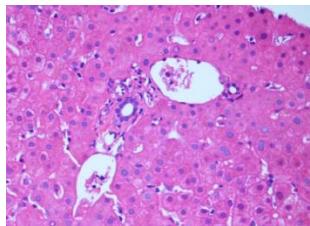
Complications associated with rejection and with immunosuppressive drugs are major causes of morbidity and mortality among organ transplant patients. Rejection occurs in about 15 to 20 percent of patients nationally after liver transplant surgery.

Several types of post-operative protocols are carried out by the Department of Pathology:

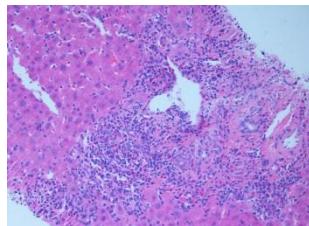
Drug analysis. Every day, under the direction of **James Faix, MD, Montefiore's Clinical Chemistry Laboratory** tests over 100 specimens from the Montefiore Einstein Transplant Center and the Children's Hospital at Montefiore for levels of immunosuppressant drugs. Most need to be tested for **tacrolimus**, a drug that inhibits the proliferation of T lymphocytes, which may attack the transplanted organ. Assays for **cyclosporine** (a drug with a mechanism of action similar to tacrolimus) and **sirolimus** (a drug that blocks proliferation in a different way) are also performed. These anti-rejection drugs are measured using immunoassay, so that testing can be done throughout the day and the results reported quickly.

Liver biopsy. Post-operative liver biopsies are performed by a surgical pathologist as requested by the clinician. For some patients, biopsies are required at one month, six months and 12 months following surgery.

Histology review. An essential part of the protocol is a post-operative histology review, performed by the **Anatomic/Surgical Pathology Laboratory** to monitor rejection and other complications.



Healthy liver



Acute cellular rejection

Transfusion Medicine: A Key Player in Liver Transplant Surgery at Montefiore

The Pathology Department's Blood Banking/Transfusion Medicine team, led by **Joan M. Uehlinger, MD**, plays an indispensable role in every liver transplantation procedure. The blood bank provides components for transfusion and correction of bleeding disorders perioperatively for the Liver Transplant Service. The blood bank's Apheresis Service provides plasmapheresis as part of the treatment of rejection, if needed. The critical services provided by Blood Banking/Transfusion Medicine integrate Surgical Pathology with patient care.



Joan Uehlinger, MD, director, Blood Banking/Transfusion Medicine (4th from left) and Leana Serrano-Rahman, MPH, manager, Blood Bank (4th from right) with members of their team.

Montefiore's Clinical Chemistry Lab: Precision Testing Ensures Accurate Results



Emily Cruz, a medical technician in Montefiore's Clinical Chemistry lab, prepares blood samples for tacrolimus testing (left) and loads the Architect analyzer.

Precision and accuracy are critical in tacrolimus testing. Underestimating tacrolimus levels can result in prescribing unnecessarily high doses of medication that can be toxic to the transplanted organ and cause debilitating side effects for the patient. Overestimating can lead to poor immunosuppression and, ultimately, organ rejection.

The lab performs four runs per day, each consisting of about 24 samples. Results are usually available within 2 hours.

Blood samples are analyzed by the Architect, a high-tech instrument that uses an immunoassay technique called **chemiluminescence** to show the concentration of the anti-rejection drug in the blood. During this process, the antigen or antibody is labeled with a molecule capable of emitting light during a chemical reaction; the light is used to measure the formation of the antigen-antibody complex.

Test results are reported to the clinician via the Soft and Epic systems.

“Any test we do, we know it can save lives,” says **Irene Ostrovsky**, senior supervisor, Chemistry Quality Assurance & Quality Control. “Whenever I visit the intensive care unit at the Children’s Hospital at Montefiore and see the very young children waiting for their transplants, it reminds me of the importance of what we do in our lab. It’s very rewarding work.”