The Cancer Letter

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How a New Jersey hospital used a misguided study of robotic surgery to wage an ill-fated war on breast cancer

By Matthew Bin Han Ong and Paul Goldberg

Using a da Vinci robot for breast cancer surgery? Is it safe? Effective?

You might want to know that, according to informed consent documents for a study that was approved by the IRB at Monmouth Medical Center, all issues stemming from robotic mastectomy have been sorted out:

"You are being asked to participate in this observational study because you are planning to undergo a robotic nipple-sparing mastectomy (RNSM) either for preventative or therapeutic purposes. This procedure has been tested and found successful for the treatment or prevention of breast cancer. You will not be asked to participate in any experimental procedures."

FDA begs to differ. The agency has not cleared the da Vinci Surgical System—the premier device for robotic surgery—for use in treatment or prevention of breast cancer.

Top-tier academic institutions disagree as well. Memorial Sloan Kettering Cancer Center recently reached consensus that the safety of robotic-assisted mastectomy for cancer treatment has not been demonstrated, and researchers at MD Anderson Cancer Center believe that there is enough equipoise around the procedure to

justify a large, multicenter randomized trial (The Cancer Letter, April 5).

Folks at the New Jersey hospital apparently felt that, with the pesky issues of safety and efficacy declared resolved, they could justify running an "observational study" focused on patient satisfaction with robotic nipple-sparing mastectomy. The hospital also advised the study's principal investigator, Stephen A. Chagares, a practicing surgeon who has no clinical trials experience, that FDA review was "not applicable."

Well, not quite. In response to questions from The Cancer Letter, FDA said the investigational use of robotic devices in mastectomy procedures would require review by the agency (The Cancer Letter, April 5).

"Wow. I cannot imagine that the hospital thought an Investigational Device Exemption from the FDA wasn't required. I don't understand that," Rita Redberg, a cardiologist and professor of medicine at the University of California San Francisco, said to The Cancer Letter. "They weren't only throwing the surgeon under the bus, they're throwing their patients under the bus, too."

Monmouth, a hospital with over 500 beds, is a teaching affiliate of the Rutgers Robert Wood Johnson Medical School and a member of the RWJBarnabas Health system. The robotic mastectomy protocol, which received IRB approval on Aug. 15, 2018, was designed to collect patient satisfaction data in the short term as well as outcomes data over 10 years. Up to 50 patients were to be enrolled.

Launching this wow-inspiring effort was the beginning of an ordeal that, according to internal documents and emails obtained by The Cancer Letter, kept getting increasingly weird.

Last October, after two patients—a woman with breast cancer and a man who experienced rapid growth of painful breast tissue—underwent robotic mastectomies at Monmouth, local press declared their treatment a potential "breakthrough."

One reader, Hooman Noorchashm, a surgeon and patient advocate who has been asking tough questions about oncologic safety of several new directions in surgery, wrote a pointed email to Michael Diamond, a reporter who wrote the story for the Asbury Park Press.

It appears that the letter made its way to the executive suite at Monmouth, causing alarm that the hospital might have a problem.

"In November 2018, Dr. Chagares' surgical coordinator tried to schedule an RNSM procedure for a risk-reducing patient. That was the first verbal notification where the hospital informed our group that the procedure was put on hold, without any written confirmation," said Nicholas Fotopoulos, a research coordinator on Chagares's team and an undergraduate student at Princeton University who was involved in the development of the Monmouth protocol.

"[The hospital administration] confirmed via telephone to Dr. Chagares that all RNSMs are completely halted, with no specifics as to why," Fotopoulos said. "I received from that point a phone call from Dr. Chagares, informing me what he had just been told. He said the hospital was concerned by a letter from Dr. Hooman Noorchasm, and I also read the news and the article that was published in the Asbury Park Press."

A conversation with Fotopoulos appears here.

Few if any protocols list emails to reporters at local newspapers among pre-specified reasons for ending a study involving human subjects. Noorchashm confirmed that he had contacted Asbury Park Press.

"I basically told the reporter that he had written an infomercial," Noorchashm said to The Cancer Letter. "I told him that he had not done enough research. I never directly contacted the medical center. He sent my email to the hospital, which was the right thing to do."

Months after enrolling several patients in a surgical outcomes study that isn't designed to assess the safety and efficacy of robotic mastectomy, Monmouth officials publicly announced a moratorium on the procedure in December 2018, citing "safety concerns." (The Cancer Letter, April 5).

Usually, when hospitals stop studies, they inform the investigators and patients. Alas, this didn't happen at Monmouth.

To date, hospital administrators have not provided written justification for the hospital's decision to end the study—leaving surgeons, principal investigators, and

patients in the dark as to what the alluded-to "safety concerns" might be.

"This is unacceptable," said Arthur Caplan, the Drs. William F. and Virginia Connolly Mitty Professor of Bioethics at New York University Langone Health and the founding director of the Division of Medical Ethics. "When you're partnering with someone, you don't abruptly end a study without explaining why, without explaining follow-up options, what's going to happen. Are you going to track the people that were in the study, or are you just leaving them in the lurch?"

This was followed by another surprising plot point.

After The Cancer Letter's initial story on robotic mastectomy April 5, Monmouth's chief medical officer, Tom Heleotis, instructed the study's lead PI and surgeon Chagares to stop collecting data.

"All data and study materials related to this protocol must be securely maintained for a minimum of three years; and there should not be any collection of any additional data on the subjects already enrolled," Heleotis wrote to Chagares in an email April 15. Several hospital executives were on the cc: list.

The Cancer Letter sent 64 questions over the past two months to Monmouth, but the hospital has not provided substantive responses to any of these questions, assuring us only that patient safety is their "paramount concern." Our questions and corrigendum to the April 5 story appears here.

"Of paramount concern to Monmouth Medical Center (MMC) is patient safety," the hospital said in a statement April 10 and May 30 to The Cancer Letter. "After an evaluation of the robotic mastectomy procedure, MMC promptly suspended the procedure, pending additional investigation of its risks and benefits."

Chagares declined to speak with The Cancer Letter in detail, citing non-disclosure agreements and attorney's advice.

"Hospital leadership vetted the process the hospital had me follow from the start and re-vetted the process just before the robotic assisted mastectomy I performed when Dr. [Antonio] Toesca [an Italian surgeon who pioneeered the robotic procedure] arrived from Italy," Chagares said in an email to The Cancer Letter May 30.

Surgeon Steven A. Chagares was the PI on an ill-fated study of robotic mastectomy at Monmouth Medical Center.

"Please note that I am at equipoise on robotic mastectomy. I would have been happy to conduct a randomized trial or take part in one. Through this process, I have relied on the directions of the IRB process and guidance from the hospital. I have been explicitly instructed not to communicate with the press throughout this ordeal. I am confident that the hospital and the IRB committee will take this opportunity to answer your important and valid questions."

Fotopoulos, the research coordinator who had worked for Chagares, said the surgeon received no "written official communication as to why a complete moratorium was placed on the procedure."

"We were told to not follow up with those patients; no additional collection of data. That's greatly concerning. It's definitely a threat to patients' health," Fotopoulos said. "Despite these instructions, Dr. Chagares is still following the patients very closely, as he does with all his mastectomy patients, as is the medical standard of care. If Dr. Chagares were to follow through with those instructions, collect no more data, to not observe the health outcomes of your patients—that would be totally inexcusable."

The directive to stop collecting data is even more disturbing, bioethicist Caplan said.

"If you're going to say, 'We're shutting down for safety reasons,' you cannot, must not, leave the subjects or the

PI in the lurch," Caplan said to The Cancer Letter. "They see that reported somewhere, they're going to call the PI and say, 'What's going on?'

"Plus, you need to know if there are any adverse events in the study group after the study ends. Who do they report to? Who do they tell? Who is paying? Should something happen, it doesn't mean that, when you shut the study down for safety issues, there's not going to be a safety issue in a year for somebody."

IDE: "N/A"

Monmouth's handling of the controversy surrounding robotic mastectomy—amidst ongoing debate on cancer-related surgical outcomes—has implications for federal policy on regulation of surgical devices.

How much rigor should be required when surgeons innovate?

In conversations with The Cancer Letter, breast surgeons at MSK and the University of Pennsylvania said they concluded that there are no prospective clinical trial data demonstrating that robotic mastectomy doesn't worsen cancer-related outcomes (The Cancer Letter, April 5).

FDA concurs. In response to the growing use of robotically-assisted surgical devices as well as in response to questions from The Cancer Letter, on Feb. 28, the agency issued an advisory that states:

"The FDA is issuing this safety communication because it is important for health care providers and patients to understand that the safety and effectiveness of using robotically-assisted surgical devices in mastectomy procedures or in the prevention or treatment of cancer has not been established."

In the Feb. 28 advisory, FDA indicated that device manufacturers looking to market surgical tools for use in the prevention or treatment of cancer may now be required to study long-term oncologic endpoints in surgical trials "for time periods much longer than 30 days."

"There is limited, preliminary evidence that the use of robotically-assisted surgical devices for treatment or prevention of cancers that primarily (breast) or exclusively (cervical) affect women may be associated with diminished long-term survival," FDA states in the advisory (The Cancer Letter, March 1).

The agency considers robotic mastectomies to be of "significant risk," which means surgeons and institutions are required to seek an Investigational Device Exemption from the agency to study the procedure on-protocol, FDA officials said.

"While individual health care providers may make individual treatment decisions in the best interests of their patients, any health care provider or health care facility formally studying the safety and effectiveness of the da Vinci for mastectomy would be expected to have an IDE," FDA said to The Cancer Letter.

Hospital administrators advised Chagares's team that an IDE was not necessary, Fotopoulos said.

"The hospital gave us a checklist of everything you need for the protocol to be approved, and one of those items was an IDE," Fotopoulos said to The Cancer Letter. "In the initial consultation meeting, the question of whether an IDE was necessary came up, and we were advised that an IDE was not required. The answer to the question became 'Not Applicable' on the application from there forward."

Fotopoulos's account of events is corroborated by a document labeled "MMC IRB Research Study Review Application," which lists the protocol title as "An Observational Study Evaluating Patients' Satisfaction After Robotic Nipple-Sparing Mastectomy."

The protocol approved by Monmouth's IRB isn't calibrated to demonstrate that the use of a robotically-assisted surgical approach would be "successful" for the treatment or prevention of breast cancer, UCSF's Redberg said.

"A single-arm observational study just at this one hospital? How would they know if this study was successful?" Redberg said. "They're doing a research study for an investigational use on an unapproved indication? So, the IDE should be applicable. I don't know how an IRB could state otherwise."

As it appears, the "observational study" was primarily designed to assess patient satisfaction after robotic mastectomy.

"A trial on robotic surgery would have to have an aim and some way of testing it, other than patient satisfaction. If you look at the protocol title, the robotic surgery is not in the protocol," Rebecca Pentz, professor of hematology and oncology in research ethics at the Emory University School of Medicine, said to The Cancer Letter. "It's all about how the patients felt about it. They're not testing robotic surgery, they're testing patient satisfaction. The endpoint is patient satisfaction."

Generally, it's legal to use a drug or a device in an indication that has not been cleared or approved by FDA, because the agency doesn't regulate the practice of medicine. Also, IRBs have the authority to make independent decisions about whether an "off-label" use poses "significant risk" to patients—although legal experts generally prefer an FDA determination over an IRB's opinion.

Nevertheless, using a drug or device off-label without an IRB-approved protocol, without sponsorship from the product manufacturer, and without an IDE, may expose the practitioner and the provider institution to legal liability.

Internal documents indicate that the Monmouth study is classified as "non-funded research," which means that the hospital did not receive funding from Intuitive Surgical to use its da Vinci robots in mastectomy procedures.

If a surgeon wants to use a device that's already on the market for an indication that hasn't been cleared or approved by FDA—without funding from a device manufacturer for a formal investigation at the institution—the hospital becomes the sponsor, said Jerry Castellano, corporate director of Institutional Review Boards at the Helen F. Graham Cancer Center and Research Institute, Christiana Care Health System.

"If I decide to get something from a company and I want to use their device in a different way, it puts all the liability on the institution," Castellano, an adjunct associate professor at the University of Delaware, said to The Cancer Letter. "That's a real key factor. The company can say, 'Hey, you did it without following our approval, and therefore you're assuming the liability for doing this.'"

Additionally, Monmouth's statement to patients that robotic mastectomy is "successful" for the treatment or prevention of breast cancer is not only unethical—patients can also sue if their cancer recurs, or if they develop cancer later in life, Castellano said.

"I think this might be a cause for potential litigation," Castellano said. "If the hospital promised that this is going to cure their breast cancer and the patient has a recurrence, it's a bit of a problem.

"That is so unethical, to put something like that in writing and present that to a patient. If they're saying it's been tested, well, show me where. That's really bothersome for a facility to do that."

Christiana would never perform experimental procedures like robotic mastectomy without an IRB-approved protocol that is powered to test long-term safety and efficacy, Castellano said.

"I could tell you, from my perspective all these years, that this would be considered to be completely unethical, and it would not get through our IRB here at Christiana," Castellano said.

Most IRBs will consult with FDA before concurring with a study sponsor that a device is non-significant risk for use in a clinical investigation, if the IRB is uncertain, said a Washington, D.C., attorney who regularly represents device manufacturers and pharmaceutical companies and who has experience with government compliance investigations and enforcement actions.

"That's often the case," the attorney said to The Cancer Letter. "I imagine there's a range of things that are obvious, but if they're in doubt at all, they're going to want FDA feedback [on whether the device is significant risk or non-significant risk]. So, they will often check with FDA."

A misleading consent form would subject a hospital to liability under common law and tort law, said the attorney, who asked not to be named, because his firm also represents many hospitals and academic medical centers.

"If you assume, hypothetically, that a hospital provided a consent form that is misleading, that would be grounds for potential liability," he said.

Laura Weber, a patient from Illinois who was scheduled to undergo prophylactic robotic mastectomy at

Monmouth in January, said the hospital never explained why she could no longer receive the surgery.

"A month before my surgery, Dr. Chagares advised me that the hospital 'halted this operation due to safety concerns,'" Weber wrote in a May 9 email to The Cancer Letter. "The news of this decision was devastating to me. Dr. Chagares and I continued to await notification from the hospital about their concerns, but no information was ever supplied to us.

"As a patient who was given zero voice or any explanation regarding the elimination of robotic mastectomy, I can't help but feel like their goals are more aligned with financial gain rather than patient care," Weber said. "Here, it is May, and I am still waiting for some type of response from the hospital as to why this option was tabled."

In an email response to Weber, Chagares wrote: "As far as the hospital, I have done everything in my power to obtain a letter of clarification defining 'safety concerns' without success … I stay committed to keeping you informed with any information as I am updated."

Similarly, patients who enrolled in the protocol and underwent robotic mastectomy didn't receive an explanation from the hospital, Fotopoulos said.

"With every change to a clinical trial, typical protocol dictates that you should be given written notification of the change," Fotopoulos said. "To my knowledge, no one has received written notification of that decision by the hospital.

"Looking back now, I experienced Monmouth Medical Center being very enthusiastic about RNSM. They were instrumental in the extensive IRB clinical trial approval process. With all the work that went into development of this clinical trial to obtain their IRB approval, to be very quickly halted, it doesn't make sense."

The hospital's instruction to stop collecting data is troubling, USCF's Redberg said.

"Certainly, medical records are a legal document, and the first thing anyone would ask for in any legal proceeding," Redberg said. "But, by trying to make sure that there isn't any information—because you think it might be damaging to the hospital—conflicts with what should be our main priority, the safety of the patients."

Monmouth's IRB doesn't have an exemplary track record. In October 2015, the hospital received a warning letter from FDA over "concerns about the adequacy of the IRB's review process."

A review by the agency concluded that Monmouth "did not adhere to FDA regulations governing the protection of human subjects," and found that the hospital's IRB:

- Failed to determine at the time of initial review that studies involving children are in compliance with 21 CFR part 50, subpart D, Additional Safeguards for Children in Clinical Investigations,
- Failed to review proposed research at convened meetings at which a majority of the members of the IRB are present, including at least one member whose primary concerns are in nonscientific areas, and
- Failed to prepare and maintain adequate documentation of IRB activities, including minutes of IRB meetings.

According to the Code of Federal Regulations and an FDA guidance for IRBs and clinical investigators, "protocol amendments must receive IRB review and approval before they are implemented, unless an immediate change is necessary to eliminate an apparent hazard to the subjects. Those subjects who are presently enrolled and actively participating in the study should be informed of the change if it might relate to the subjects' willingness to continue their participation in the study."

Going forward, such problems at Monmouth would be less likely to occur, at least on the oncology side. As of May 2019, all cancer-related clinical trials in the RWJBarnabas Health system are required to undergo review by the Rutgers Cancer Institute of New Jersey. Cancer-related trials will go through scientific and feasibility review and receive approval prior to IRB review.

Misplaced trust

Chagares is a busy general, laparoscopic, and breast surgeon who has no experience with clinical trials.

Clearly, he got excited by the innovative use of da Vinci robots in breast surgery, and he hired Fotopoulos to

handle the paperwork and interactions with the Monmouth IRB.

The surgeon appears to have trusted Monmouth—after all, he was trained there, and has been affiliated with the hospital throughout the 20-plus years that he has been in practice as a surgeon.

This isn't a story about a rogue physician armed with a robot and a surgical personality—as The Cancer Letter's April 5 story on robotic mastectomy may seem to suggest. In fact, Chagares appeared to have followed directives from hospital administrators in a measured way, asking the right questions and applying pressure at the right moments, internal documents and correspondence obtained by The Cancer Letter show.

In the course of reporting the April 5 story, an inside source informed The Cancer Letter that Chagares performed robotic mastectomy on patients without a protocol and without oversight.

This, we later learned, was inaccurate.

Paul Goldberg, editor and publisher of The Cancer Letter, tells how this story grew out of a correction into an investigation. His story appears here.

Documents show that, after reading about robotic nipple-sparing mastectomy in early 2018, Chagares wrote to Antonio Toesca, an Italian surgeon who pioneered the procedure, to explore training opportunities.

"Dear Dr. Chagares, I am very pleased to know that you are interested in this new surgical procedures," Toesca replied to Chagares in an email April 26, 2018. "The feasibility study on robotic nipple-sparing mastectomy with immediate robotic reconstruction was closed in February 2017 with excellent results. From March 2017, a randomized trial comparing an open surgical arm with a robotic surgery arm is underway. Currently, enrollment is ongoing and I expect to finish the study towards the end of 2018.

"If you want to approach this type of operation, you have three possibilities. The first would be to come and see surgery at the European Institute of Oncology in Milan as an observer in OR."

Enthused, Chagares recruits Fotopoulos as research coordinator, and the two leave for Milan on June 4, 2018.

After observing two robotic mastectomies performed by Toesca, while still in Milan, Chagares wrote in an email to top executives at Monmouth: "The results are great! No scars on the breasts at all. The nipples stay intact. Unbelievable patient satisfaction while still removing all the breast tissue. The results are incredible. The reconstruction is done at the same time via the same 1 inch incision in the axilla.

"As a breast surgeon who has been performing breast surgery for 22 years, I am blown away. Who can I work with who will aggressively assist me in obtaining an IRB in a timely fashion?"

Eric Carney, Monmouth's chief operating officer, hit "reply all" and responded in an email June 8: "The robotic approach seems very innovative. However, we have many questions about FDA, Intuitive and IRB approvals. I agree … to work through IRB and we can model financials."

Chagares, who is certified by Intuitive Surgical to perform robotic surgery, decided that Toesca should be his proctor, at the hospital's invitation.

"Dr. Toesca, from Milan will attend the procedures as my proctor. Please confirm that this is what the Hospital would like me to do," Chagares wrote hospital administrators on June 20, 2018. "Also, can someone advise what process Dr. Toesca needs to follow in order to be the proctor."

Hospital administrators confirmed Dr. Toesca's participation as a proctor for Dr. Chagares on Aug. 6, 2018. Monmouth created a Facebook post on Sept. 14 to announce Toesca's arrival:

"MMC is proud to welcome Dr. Antonio Toesca of the Division of Breast Surgery at the IEO European Institute of Oncology, Milan, Italy," the hospital wrote on its Facebook page. "A noted authority on robotic mastectomy, Dr. Toesca traveled to MMC to observe the hospital's first robotic mastectomy procedure performed by Dr. Stephen Chagares."

As the protocol made its way through the hospital's IRB, top executives offered to engage Monmouth's local marketing firepower.

"I have forwarded to Marketing for awareness and follow up," Monmouth COO Carney wrote in an email Aug. 8.

"We would love to support Steven [sic] and assist in awareness campaign for a robotic approach. Very exciting times, thank you for pushing through IRB at MMC."

On Aug. 15, 2018, Chagares received notification that the hospital's IRB committee had voted 8-0 to approve his proposed protocol, titled, "An Observational Study Evaluating Patients' Satisfaction After Robotic Nipple-Sparing Mastectomy (IRB Registration #00003104)."

According to Fotopoulos, Chagares's original draft of the protocol was based on Toesca's Italian clinical trial, which includes cancer patients and high-risk patients who were candidates for traditional skin, nipple and areola-sparing mastectomy.

"We were also monitoring oncologic outcomes to make sure that, with regular follow up with Dr. Chagares, these patients were staying healthy, they were pleased with their cosmetic outcome, the cancer wasn't returning and the oncologic outcomes were the same or better than standard surgery," Fotopoulos said.

In the correspondence, there are no indications that Chagares and his team are aware of the fatal flaws that the IRB was introducing into his protocol.

"The IRB committee itself worked with us pretty much in every step of the way in order to design the protocol. We wanted to make sure we did everything correctly," Fotopoulos said. "The IRB committee had their own input on revisions multiple times throughout the admission process. We made every modification they requested. Monmouth Medical Center made a multitude of direct edits to the protocol, consent, and other accompanying documents until they deemed them satisfactory. Monmouth Medical Center, and the IRB committee, specifically, was with us every step to make sure that this protocol was as it should be."

The end result was a protocol that was edited, vetted, and unanimously approved by members of Monmouth's IRB, Fotopoulos said.

Mistakes were made. The person or persons who edited out the control arm from Toesca's study apparently neglected to change one of the protocol's primary hypotheses: that the use of a robotic device to perform a nipple-sparing mastectomy does not worsen the oncologic outcome of patients with breast cancer or BRCA mutation.

After being dismantled and reconstituted, the Monmouth protocol simply doesn't provide the data for a hypothesis test.

Why would Monmouth offer robotic surgery for an unapproved indication to patients without a safety and efficacy protocol, promise high-risk patients that the procedure is "successful" for use in said indication, and simultaneously enroll patients in a data collection protocol to assess whether the procedure worsens oncologic outcomes?

"This is concerning on so many levels, and it contradicts itself," Otis Brawley, Bloomberg Distinguished Professor of Oncology and Epidemiology and associate director for community outreach and engagement at the Bloomberg School of Public Health and Johns Hopkins Kimmel Cancer Center, said to The Cancer Letter.

Patients shouldn't participate in research that's not going to answer a scientifically valid question, Emory's Pentz said.

"If you have a study which is hypothesis-driven, and if you have to close the study when your sample size is too small to get any good data—and if the follow-up data will not provide useful scientific information—then you should not continue to collect protocol data," Pentz said. "The courteous thing to do would be to say, thank you participating in our trial, unfortunately we've had to stop, we won't be calling you in the future, we still appreciate your help."

"IRB ACTION: Closed"

Internal documents and correspondence show that least six top executives at Monmouth had in-depth knowledge about the adoption of robotic mastectomy procedures at the hospital, as well as the evolution of Chagares's protocol, from conception to termination:

- Bill Arnold, president and CEO
- Eric Carney, chief operating officer
- Tom Heleotis, chief medical officer
- Joseph Jaeger, associate vice president of academic affairs and acting chair of the Institutional Research Review Board

- Barbara Mihelic, director of clinical research – IRB
- Manpreet Kohli, director of breast surgery

"When you first reached out, Dr. Chagares referred to the hospital administration, and they said there were very strict media guidelines for IRB clinical trials and he was told not to speak with The Cancer Letter," Fotopoulos said. "I believe you reached out to Dr. Chagares again, and he was again told not to speak with the media, specifically The Cancer Letter, as per the hospital administration's instruction."

Because of Monmouth's public statements on "safety concerns," the hospital's leadership has an even greater responsibility to communicate with Chagares and his patients, UCSF's Redberg said.

"For a hospital to announce the safety concerns, the hospital is certainly, morally and ethically obligated to inform the patients, and state what the safety concerns are," Redberg said. "I cannot imagine a good reason why you would not follow up when you have concerns about safety. That would be all the more reason to do close and careful follow-up."

On Dec. 17, 2018, Chagares formally requested closure of the protocol.

"We are currently unable to perform robotic nipple-sparing mastectomies at Monmouth Medical Center and therefore do not have any patients who meet the inclusion criteria outlined to be enrolled in this observational study," Chagares wrote in the letter to Monmouth's IRB. "At this time, we are not able to enroll any patients and would like to close this study."

The hospital responded two months later, on Feb. 13, 2019.

"To advise you that the above referenced Study has been presented to the Institutional Review Board identified above, and the following action taken subject to the conditions and explanation provided below," Monmouth's Jaeger wrote in a letter from Arnold's office.

Below this statement, an annotation read: "IRB ACTION: Closed." There were no "conditions and explanation" provided.

How does this protect the patients?

"The IRB should be demanding that written communication occur to the subjects with an explanation of what's going on and what their rights are," NYU's Caplan said. "If someone is harmed or suffers harm later, and they have not had follow up, there is going to be significant liability.

"At this point in time, the standard of practice for recruiting subjects is to not only bring them in and discuss their options, but tell them when and what will happen if the study has to close prematurely."

Monmouth should have negotiated the shutdown of the study with Chagares, because as the surgeon and lead PI, he is responsible for the enrolled patients, Caplan said.

"That means the PI has to be fully informed," Caplan said. "We used to treat patients under the banner of 'subject,' and because we so eager to get people to come into research in oncology, but other areas, too, the notion has emerged in the past few years that people are to be treated as partners, co-equals, collaborators. This [hospital's] behavior isn't consistent with that."

These standards apply, whether patients are enrolled in a randomized clinical trial or an observational study, Caplan said.

"It doesn't matter, it applies to everyone," Caplan said. "The failure to have an exit strategy is unacceptable in 2019."