History of the Surgical Research Laboratory of the University of Puerto Rico

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Objective: The history of the University of Puerto Rico (UPR) Surgical Research Laboratory was reviewed from its founding in 1952, by Dr. Francisco Raffucci, to the present.

Method: The information for this overview was obtained from the annual reports written by the surgical laboratory directors. Interviews with surgeons who worked in the early facilities, and published works, provided the early history for which no annual reports were available.

Results: The history of the laboratory begins at the former School of Tropical Medicine, under the direction of Dr. Francisco Raffucci (1952–1964). The laboratory was housed in a small building on the school grounds. Research in cardiovascular surgery, shock and transplantation was performed and published. The facility was later moved to a wooden building at the Medical Center, a medical complex in San Juan, Puerto Rico and was directed by Dr. Leovigildo Cuello (1964–1967), followed by Dr. Gerhart Ramírez Schon (1969–1972). Under Dr. Eduardo Santiago-Delpín (1972–1977) the laboratory was moved to the tenth floor of the UPR School of Medicine. Subsequent directors of the laboratory at the school of medicine were Dr. Pedro Roselló (1977–1983), Dr. Norma Cruz (1983–2004), Dr. Manuel Más (2000–2015), Dr. Aura Delgado (2015–2017), Dr. Enrique Márquez (2017–2018) and Dr. Anwar Abdul-Hadi (2018–2024), who still leads the laboratory. Currently, the facility is used in collaboration with equipment manufacturers as a surgical simulation center and on various research.

Conclusion: The Surgical Research Laboratory continues training surgeons to use new surgical devices and supporting research projects.

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Advances in the field of surgery have largely been achieved in surgical research laboratories (1). Myocardial revascularization (2), extracorporeal circulation (3-4), and organ transplantation (5), were all developed in a laboratory before being used in patients. In the United States structured surgical research laboratories were first established in 1942 at the Johns Hopkins Cardiac Surgery Research Laboratory (1); in Puerto Rico (PR) our facility started in 1952.

As we approach the 75th anniversary of the founding of the University of Puerto Rico (UPR) School of Medicine in 1950, to be commemorated in 2025, preserving the histories of our research units has become increasingly important.

Methods

The information for this historical review was obtained from the annual reports that were written (beginning in 1970) by the directors of the Surgical Research Laboratory. Copies of these reports were preserved at the facility, and we were allowed to examine them. Interviews with some of the surgeons who worked at the laboratory in the early years—such as Dr. Marino Blasini, who was the first resident to rotate into the laboratory (Fig 1)—were of great help. Finally, information collected by Dr. Vázquez-Quintana and published in his book (6) on the history of surgery in PR completed our sources of information.

Results

Francisco Raffucci Arce, MD, 1952–1964

The first director and founder of the Surgical Research Laboratory was Dr. Francisco Raffucci. He studied medicine at the University of Maryland (1940-1943) and later trained in general surgery at the Hospital of Tropical Medicine, under the direction of Dr. José Noya Benítez. He completed a fellowship in cardiovascular surgery at the University of Minnesota under Dr. Owen H. Wangensteen and returns to PR with the expertise required to establish a surgical research laboratory.

A small concrete building located at the north entrance of the courtyard of the School of Tropical Medicine, was converted into the Surgical Research Laboratory. Dr. Raffucci adopted the research approach of the University of Minnesota, and his mentor Dr. Owen Wangensteen. Mongrel dogs were used as the preferred animal model for surgical research in cardiovascular surgery, organ transplantation, shock and hepatic perfusion.

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Figure 1. Dr. Marino Blasini (right, 96 years old) during our interview for this historical overview. He did his surgery residency training between 1956 and 1960 under the direction of Dr. Raffucci and performed research at the Surgery Research Laboratory. With him are Dr. Eduardo Santiago Delpín (left) and Dr. Norma Cruz (center).

Among the many surgeons who worked there and published scientific studies were Gumersindo Blanco, David Rodríguez-Pérez, Alberto Adam, Rafael Sorrentino, José Bernal, and Marino Blasini.

The peer-reviewed scientific publications from Dr. Raffucci and his group that period (1952–1964) are shown in Table 1-A. Dr. Raffucci's work with Dr. Eiseman was cited 48 times.

Leovigildo Cuello Mainardi, MD, 1964–1967

In 1960 the clinical faculty of the UPR School of Medicine moved from the Municipal Hospital in Santurce to a new location at the Medical Center, a government-run medical complex in Río Piedras. Since the faculty needed to be close to the Surgical Research Laboratory, the facility was moved to the new site. The selected place was a wooden structure on the north side of a building known as the Center for Clinical Investigation. The area was located in what is now the Pediatric Hospital.

Dr. Raffucci appointed Dr. Leovigildo Cuello the new director of the facility in 1964. Dr. Cuello had a medical degree from the University of Paris in France (1949–1956). He completed his internship at the Municipal Hospital (1955–1956) and his general surgery training in the UPR program (1957–1961). He later traveled to the University of Minnesota where he trained in cardiovascular surgery (1961–1963) and obtained a master's degree in surgical sciences.

One of Dr. Cuello's priorities was cardiovascular research, and he produced multiple publications in this field. Table 1-B has a list of the peer-reviewed publications from 1964 through 1967.

Gerhart Ramírez Schon, MD, 1969–1972

In 1969 the directorship of the Surgical Research Laboratory was given to Dr. Ramírez Schon. The new director had completed his medical training at the UPR School of Medicine (1956–1960), and his internship at the UPR University Hospital (1960–1961) and had started general surgery residency in the UPR Program (1961–1964). His training was interrupted by military service, but upon returning he completed general surgery residency (1966–1968).

As a resident Dr. Ramírez had a one-year (1963–1964) rotation at the Surgical Research Laboratory where he developed the expertise needed to run the facility.

The peer-reviewed publications for the 1969–1972 period are shown in Table 1-C.

Eduardo Santiago Delpín, MD, 1972–1977

In 1972 the UPR School of Medicine moved from San Juan to a new building at the Medical Center in Río Piedras, and the Surgical Research Laboratory occupied the 10th floor of this building (Figs. 2-a and 2-b). The physical facilities available to the Surgical Research Laboratory included five operating rooms, a recovery room, an animal preparation room, a radiology suite, and areas for the sterilization of instruments.

Dr. Eduardo Santiago-Delpín, who trained in general surgery in the UPR program (1965–1970) and later in organ transplantation in the University of Minnesota program (1970–1972) was appointed chief of the new Surgical Research Laboratory by Dr. Víctor Gutiérrez, then chief of the Surgery Department.

The peer-reviewed publications that resulted from experimental studies performed at the laboratory during this period are shown in Table 1-D.

Residents were offered research and technical rotations to stimulate investigative work. Third-year medical students rotated through the surgical research facilities for technical exercises on suturing techniques and instruction in basic areas of surgery.

Pedro Rosselló González, MD, 1980–1983

Dr. Pedro Rosselló completed his training in general and pediatric surgery at Harvard, and returned to PR in 1976. He began working in the Pediatric Surgery Section of the UPR Surgery Department, and was appointed chief of the Surgical Research Laboratory by Dr. Gumersindo Blanco, then chief of surgery. He assumed the new position in 1980.

In 1981, a major reorganization shifted the laboratory's supervisory responsibilities to the Animal Resource Center. This reorganization included the transfer of the main responsibility for both animal care and the large-animal cage area, previously under the laboratory's supervision, to the Animal Resource Center.

Table 1. Publications of the Surgical Research Laboratory during the different periods and the number of citations as indicated by Pub Med.

	Times Cited
A. Dr. Francisco Raffucci (1952-1964)	
1. Raffucci FL. The effects of temporary occlusion of the afferent hepatic circulation in dogs. Surgery 33:342-351, 1953.	13
2. Raffucci FL, Lewis FJ, Wangensteen OH. Hypothermia in experimental hepatic surgery. Proc Soc Exp Biol Med. 83:639-640, 1953.	8
3. Cross FS, Raffucci FL, Brackney EL, Wangensteen. Relationship of prolonged drainage of bile through pancreatic duct system to pancreatitis. Proc Soc Exp Biol Med. 90:208-210, 1955.	4
4. Adam A, Blanco G, Raffucci FL, Fernandez A. Direct experimental approach to the aortic valve. J Thorac Surg. 31:359-363, 1956.	0
5. Blanco G, Adam A, Fernandez A. A direct experimental approach to the aortic valve. II. Acute retroperfusion of the coronary sinus. J Thorac Surg. 32:171-177, 1956.	4
6. Blanco G, Adam A, Rodríguez Pérez D, Fernandez A. Complete homotransplantation of canine heart and lungs. AMA Arch Surg 76(1):20-23, 1958	5
7. Cullen ML, Blanco G, Nuñez LE, Rey-Baltar E, Bailey CP. Anastomosis of coronary and internal mammary arteries; an experimental study. J Albert Einstein Med Cent. 6:235-238, 1958.	0
8. Bernal-Rosa JF, Fernandez A, Raffucci FL. Effect of suture material on urinary bladder wound healing. Surgery 43:935-938, 1958.	0
9. Raffucci FL, Blasini M, Vilaro JR, Fernandez A. Prophylactic use of procaine amide (Pronestyl) in ventricular fibrillation during the production of intracardiac defects in dogs under hypothermia. Am J Surg. 102:677-679, 1961.	0
10. Oliveras FE, Garcia Reyes LF, Raffucci FL, Perez V. Fibrinolysin in the treatment of thrombosed arterial prosthetic grafts. Experimental study. Am J Surg 105:779-780, 1963.	0
11. Raffucci FL. Shock. Bol Asoc Med PR. 55:312-314, 1963.	0
12. Sorrentino RG, Cuello L, Raffucci FL. Experimental production of hemopericardium in dogs. Bol Asoc Med PR. 55:299-302, 1963.	0
13. Eiseman B, Liem DS, Raffucci F. Heterologous liver perfusion in treatment of hepatic failure. Ann Surg 162:329-345, 1965	48
B. Dr. Leovigildo Cuello (1964-1967)	
1. Cuello Mainardi L, Raffucci FL, Electrical Conversion of atrial fibrillation with a direct current shock. Bol Asoc Med PR 56:288-290, 1964.	0
2. Mainardi LC, Rodríguez Pacas G, Raffucci FL. Surgical treatment of mitral valve disease. Bol Asoc Med PR. 56:334-341, 1964.	0
3. Cuello L, Vázquez-Quintana E, Gutierrez VS, Raffucci-Arce FL. Determination of the optimum flow during ex-vivo liver perfusión. Surg Forum 16:290-293, 1965.	0
4. Ramirez Schon G, Raffucci FL, Cuello L, Perez Cintron V. Variations in hemoglobin concentration in large blood vessels in dogs. J Surg Res 5:123-126, 1965.	0
5. Cuello L, Vázquez E, Pérez V, Raffucci FL. Autologous blood transfusión in cardiovascular surgery. Bol Asoc Med PR. 58:93-101, 1966.	0
6. Cuello L, Vázquez E, Raffucci FL, Pérez V. Autologous blood transfusión in cardiovascular surgery. Transfusion 7:309-315, 1967.	5
7. Cuello L, Vázquez E, Ríos R, Gutiérrez V, Raffucci FL. Peritoneal dialysis in pancreatitis in dogs. Bol Asoc Med PR. 59:237-242, 1967.	0
8. Cuello L, Vazquez E, Rios R, Raffucci FL. Autologous blood transfusión in thoracic and cardiovascular surgery. Surgery 62:814-818, 1967.	0
C. Dr. Gerhart Ramírez Schon (1969-1972)	
1. Santiago Delpín EA, Ramírez Schon G, Rodríguez Millán P, Oliveras FE, Pérez Cintrón V. Postoperative infection in dogs. Bol Asoc Med PR. 61:436-439, 1969.	0
2. Santiago Delpín EA, Rodríguez Millán P, Rodríguez OL, Ramírez Schon G, Raffucci FL. The use of a new polyglycolic acid suture in general surgery: clinical and experimental studies. Bol Asoc Med PR. 62:309-312, 1970.	0
3. Raffucci FL, Ramírez-Schon G. Management of tumors of the liver. Surg Gynecol Obstet 130:371-385, 1970.	0
4. Just-Viera JO, Rivé-Mora E, Altieri PI, Girod CE. Tricuspid atresia and the hypoplastic right ventricular complex: complete correction for long term survival. Surg Forum 22:165-166, 1971.	0
5. Just-Viera JO, Rive-Mora E, Rodriguez OI, Altieri P and Girod CE. Atriopulmonary Shunt. Ann Thorac Surg 15:41-49, 1973.	0
D. Dr. Eduardo Santiago Delpín (1972-1977)	
1. Santiago-Delpín EA, Yunis E, Callender CO, Najaria JS. The immunologic effect of chlorphenesin on skin grafts in normal and thymectomyzed mice. Cell Immunol 5:604-607, 1972.	0
2. González A, López R, Santiago-Delpín E, Just Viera JO. Protection of the lung during experimental contusion. Bol Asoc Med PR. 67:317, 1975.	0
3. Santiago Delpín EA, Figueroa I, López R, Vázquez J. Protective effect of steroids on liver ischemia. Am Surg. 41:683-685, 1975.	14
4. López R, Suárez A, Santiago-Delpín EA. A reversed jejunal segment interposition as feeding gastrostomy. Arch Surg. 112:343-344, 1977.	1
5. Santiago-Delpín EA, Szepsenwol J. Prologed survival of skin and tumor allografts in mice on high-fat diets. J Natl Cancer Inst. 59:459-461, 1977.	0
6. Santiago-Delpín EA, Suárez A, Vivoni V. Pharmacological protection of ischemic organs. Transplant Proc 9:1583-1585, 1977.	0
7. González A, López R, Figueroa I, Santiago-Delpín EA, Just-Viera JO. Glycerol in experimental lung contusion. Surg Forum 28:176-177, 1977.	0
8. Román-Franco AA, Santiago-Delpín EA. The immunoregulatory role of cholesterol and other lipids: a hypothesis. Med Hypotheses 3:235-240, 1977.	1
9. Lowry P, Blanco T, Santiago-Delpín EA. Histamine and sympathetic blockade in septic shock. Am Surg. 43:12-19, 1977.	1
10. Santiago-Delpín EA, Vivoni V, Suárez A, Román-Franco AA. Protection of organs during experimental ischemia. Surg Gynecol Obstet 147:740-744, 1978.	0

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E. Dr. Pedro Roselló (1980-1983)	
1. Rosselló PJ, Lebrón H, Franco AA. The technique of myotomy in esophageal reconstruction: an experimental study. J Pediatr Surg 15:430-432, 1980.	3
2. Lores ME, Cañizares O, Rosselló PJ. The significance of elevation of serum phosphate levels in experimental intestinal ischemia. Surg Gynecol Obstet. 152:593-596, 1981.	8
3. Lores ME, Ortiz JR, Rosselló PJ. Peritoneal lavage with povidone-iodine solution in experimentally induced peritonitis. Surg Gynecol Obstet 153:33-38, 1981.	3
F. Dr. Norma Cruz (1983-2004)	
1. Cruz NI, Blanco G, Cestero H. Preserved arterial grafts in micro-vascular surgery. J Microsurgery 2:250-252, 1981.	0
2. Cruz NI, Cestero HJ, Cora MI. Management of contaminated bone grafts. Plast Reconstr Surg 1981, 68(3):411-414.	2
3. Cruz NI, Ariyan S, Miniter P. An Experimental Model to Determine the Level of Antibiotics in Irradiated Tissues. Plast Reconstr Surg 73:811-816, 1984.	0
4. Cruz N, Debs N, Fiol RE. Evaluation of Fibrin Glue in Rat Sciatic Nerve Repairs. Plast Reconstr Surg 78:369-373, 1986.	18
5. O'Neil J, Lowry P, Cruz NI. Inhibition of Vasoactive Substances in Experimental Endotoxin Shock. PR Health Sci J 5:7-11, 1986.	0
6. Matos M, Cruz NI. Reversing the Detrimental Effect of Adriamycin on Skin Grafts in Rats. Plast Reconstr Surg 80:591-594, 1987.	0
7. Rodríguez-Bigas M, Cruz NI, Suárez A. Comparative Evaluation of Aloe Vera in the Management of Burn Wounds in Guinea Pigs. Plast Reconstr Surg 81:386-389, 1988.	14
8. Cruz NI, Canario QM. Muscle Flaps in the Management of Vascular Grafts in Contaminated Wounds: An Experimental Study in Dogs. Plast Reconstr Surg 82:480-483, 1988.	0
9. Rodríguez PM, Cruz NI, González CI, López R. The Effect of a High Fat Diet on the Incidence of Colonic Cancer after Cholecystectomy in Mice. Cancer 62:727-729, 1988.	2
10. Arboleda B, Cruz NI. The Effect of Systemic Isotretinoin on Wound Contraction in Guinea Pigs. Plast Reconstr Surg 83:118-121, 1989.	2
11. Cruz NI, Bayron FR, Suárez AJ. Accelerated Healing of Full-Thickness Burns by the Use of High Voltage Pulsed Galvanic Stimulation in the Pig. Ann Plast Surg 23:49-55, 1989.	5
12. Soltero E, Cruz NI, Nazario CM, López R, Alonso A, Ríos CF. Cholecystectomy and Right Colon Cancer in Puerto Rico. Cancer 66: 2249-2252, 1990.	0
13. Cruz NI, Korchin L. The effect of isotretinoin and triamcinolone acetonide on human skin fibroblasts in vitro. Plastic Surgical Forum, 16:309-310, 1993.	0
14. Cruz NI, Korchin L. Inhibition of Human Keloid Fibroblasts Growth by Isotretinoin and Triamcinolone in Vitro. Ann Plast Surg 33: 401-405, 1994.	13
15. Cruz-Korchin NI, Korchin L, Gonzalez-Keelan C, Climent C, Morales I. Macromastia: How much of it is fat? Plast Reconstr Surg 109: 64-68, 2002.	9
16. Portilla P, Cruz-Korchin N, Rodriguez I. Endotracheal intubation of large pigs: Making it simple. Bol Asoc Med PR. 97:222, 2005.	0

During this period the Surgical Research Laboratory continued its research and teaching activities.

The level of activity was maintained, however, in the face of some significant problems of funding due to the economic difficulties of the university at this time. Although the participation of surgical residents from multiple training programs increased, available resources, such as funding, personnel, and faculty, were in decline.

The research publications from this period (1980–1983) are listed in Table 1-E.

Norma I. Cruz Mendieta, MD, 1983–2004

At the beginning of the 1983–1984 academic year, Dr. Norma Cruz was appointed director of the Surgical Research Laboratory. She had completed her training in plastic surgery at Yale University, where she also conducted research on wound healing. A few months later, Dr. Enrique Vázquez-Quintana became the chief of the Department of Surgery, under which the Surgical Research Laboratory continued to operate. The laboratory shared responsibilities in the areas of teaching and research with the Department of Surgery.

The increased cost and difficulty of obtaining research animals limited the amount of research performed with animal models. The many federal regulations governing the use and care of research animals obstructed areas of surgical investigation such as cardiovascular and gastrointestinal research, neither of which can be transferred to in vitro models.

The use of animals in the laboratory continued, but to a lesser extent than formerly. Pigs became the animals most frequently used because they were readily available, served as good research and teaching models, and were non-pet animals ordinarily destined for slaughter.

In the 1990's, tissue-culture facilities were added to the Surgical Laboratory to support in vitro research studies on collagen production in keloid scars.

Additional financial support was obtained from the Department of Surgery (Plastic Surgery Service) by transferring a percentage of revenue from direct patient care to the laboratory account.

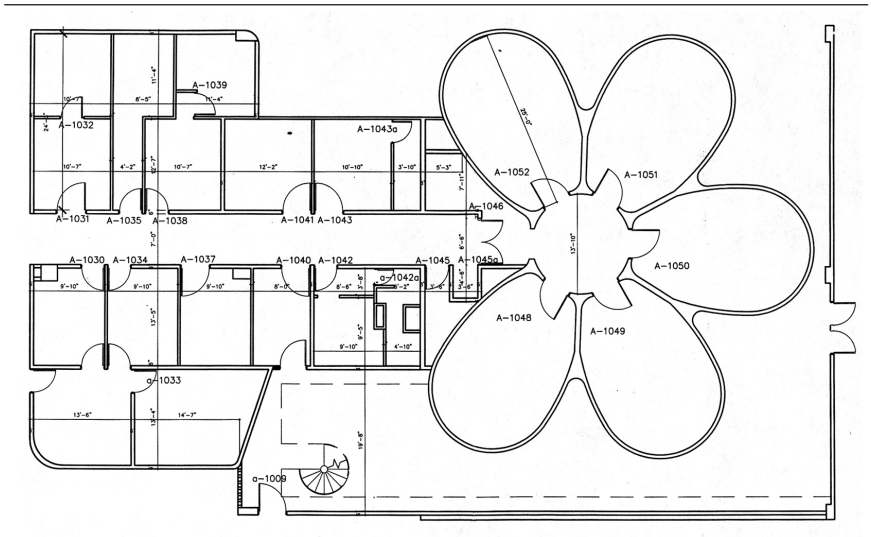
The list of the peer-reviewed publications resulting from research performed at the laboratory at this time appears in Table 1-F. Research during the first half of this period focused on animal models, whereas the second half concentrated on clinical studies.

Manuel Más Ramírez, MD, 2004–2015

In July 2004 the chief of surgery, Dr. Juan José Lojo, appointed Dr. Manuel Más director of the Surgical Research Laboratory. Dr. Más had completed his training in general surgery in the UPR program in 1985 and had trained in basic laparoscopy in 1991 in Nashville, Tennessee.

At this time, the absence of an allocated fixed budget from the School of Medicine for operational expenses was a significant weakness of the Surgical Research Laboratory. In an effort to

Figures 2a and 2-b. (a) Floor map of the Surgical Research Laboratory at the UPR School of Medicine (10th floor), with its five operating rooms. (b) Entrance to the Surgical Research Laboratory.



achieve fiscal stability, the facility negotiated with equipment manufactures to offer, for a reasonable fee, courses on how to perform new laparoscopic techniques with the most modern surgical equipment. Laparoscopic surgical skills were new and simulation laboratories where such skills could be learned in a protected environment were needed.

By 2011 the Surgical Research Laboratory had become a self-sustained unit, in terms of its operational budget, thanks to the collaborative agreements with equipment manufacturers. The surgical faculty and residents no longer used the facility to perform research projects, but to train in the new skills required to use modern laparoscopic equipment.

Aura Delgado Cifuentes, MD, 2015–2017

In 2015 Dr. Aura Delgado was appointed director of the Surgical Research Laboratory by the chief of surgery, Dr. Segundo Rodríguez Quilichini. She had trained in general surgery in the UPR program from 2008 through 2013 and had completed additional training in colorectal surgery at the State University of New York (SUNY) in Buffalo, New York (2014–2015). After returning from New York, she was assigned to supervise workshops conducted by several private companies using the pigs and fresh cadavers.

No research by the surgery faculty or residents was carried out in the facilities during this period. The Surgical Research Laboratory transitioned from a research unit to a training unit, with state-of-the art equipment for teaching surgical skills.

Enrique Márquez Grau, MD, 2017–2018

For a short period of time, Dr. Enrique Márquez, a pediatric cardiovascular surgeon, took over the direction of the Surgical Research Laboratory. Because of health problems, he stayed for only one year.

Anwar Abdul-Hadi Martínez, MD, 2018–2024

Dr. Anwar Abdul-Hadi who trained in Canada as a pediatric surgeon was appointed in 2018 as director of the Surgical Research Laboratory by Dr. William Méndez, who was the chief of surgery.

During this period the Surgical Research Laboratory became a surgical simulation center supported by a legislative grant that had been used in 2017 to obtain a simulator.

The demands for workshops, courses and certifications required by the American Board of Surgery, hospital accreditation committees, and agencies such as the Accreditation Council for Graduate Medical Education were met by the training offered at the surgical simulation center.

The slow transition from being the research workshop of the Department of Surgery to being the training workshop for acquiring new surgical skills, was completed in 2018.

Discussion

This brief historical appraisal of the surgical laboratory gives a glimpse of the role this unit had in surgical research and training. In spite of the fact that operating a well-designed (7-8) surgical laboratory is expensive, alliances with surgical equipment

manufacturers help with the operational expenses. Currently the role of the surgical research laboratory is that of training young surgeons in the new skills needed for laparoscopic surgeries.

Conclusion

In the early years of the Surgical Research Laboratory, the emphasis was on research and experimental surgery. Currently it is used mainly to train surgeons in the use of new devices. Endoscopic and robotic surgeries require skills that can be obtained only in the protected environment of a simulator laboratory.

Resumen

Objetivo: Revisamos la historia del Laboratorio de Cirugía Experimental de la Universidad de Puerto Rico (UPR) desde su fundación en el 1952 por el Dr. Francisco Raffucci hasta el presente. Métodos: Los informes anuales de los directores del Laboratorio se utilizaron para preparar este trabajo. Entrevistas a cirujanos que laboraron en esta facilidad y sus publicaciones se utilizaron para completar la información no disponible. Resultados: La historia del Laboratorio de Cirugía Experimental comienza en la Escuela de Medicina Tropical bajo el Dr. Francisco Raffucci (1952–1964). Un edificio de concreto en el patio de la escuela fue el laboratorio de cirugía. Investigación en cirugía cardiovascular, "shock" y trasplante se realizó en esta facilidad y se publicó. Más tarde el Laboratorio fue trasladado a un edificio de madera en el Centro Médico, bajo la dirección del Dr. Leovigildo Cuello (1964–1967), seguido del Dr. Gerhart Ramírez Schon (1969–1972). Bajo el Dr. Eduardo Santiago-Delpín (1972–1977) el laboratorio se traslada al décimo piso de la escuela de medicina de la UPR. Los directores de la facilidad en la escuela de medicina han sido el Dr. Pedro Reselló (1977–1983), Dra. Norma Cruz (1983–2004), Dr. Manuel Más (2004–2015), Dra. Aura Delgado (2015–2017), Dr. Enrique Márquez (2017–2018) y Dr. Anwar Abdul-Hadi (2018–2024). Actualmente, la facilidad se usa en colaboración con manufactureros de equipo como un centro de simulación quirúrgica y colabora con la investigación. Conclusión: El Laboratorio de Cirugía Experimental continúa entrenando cirujanos en el uso de los nuevos equipos y brindando apoyo a proyectos de investigación.

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