SCIENTIFIC PRODUCTION REPORT **2019**

A.C.Camargo Cancer Center
Centro Integrado de Diagnóstico, Tratamento, Ensino e Pesquisa

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SCIENTIFIC REPORT
2019

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ADMINISTRATION'S STAKEHOLDER LETTER

For us at the A.C.Camargo Cancer Center, 2019 was a year of important developments that left tangible marks on the Institution's history. The consolidation of an integrated care management model left us proud and optimistic about all the possibilities available to care for cancer patients.

Cancer is a global challenge that requires an ever-strengthening commitment on our part to make significant advances in the research that will end up offering great benefit to patients. The goal of our institution is to beat cancer, patient by patient, ethically with knowledge, resoluteness, innovation, humanity, sustainability, and focus on the patient. Our center is an institution of excellence and state-of-the-art technology with the ability to offer treatment and care alongside integrated research and education.

In 2019, we continued to introduce reference centers prepared for tumors of the head and neck, upper digestive tract, and the colorectal. This journey began in 2018 with breast, gynecological and skin tumors. Another six reference centers to be opened by the end of 2021 are in the planning stage: urological, thoracic, hematological, bone, central nervous system and pediatric tumors. In this way, we are moving forward with the consolidation of a cancer center model, which integrates care specific to each patient with scientific development and specialized staff training. With rationalized costs and processes, this model allows us to offer the right treatment at the right time for our cases using protocols designed by experienced professionals in a scrupulous and safe manner. For complex cases requiring the adaption of established protocols, we have multidisciplinary discussion forums – tumor boards – and there is the possibility of gaining access to new treatments through our research clinics, which are bringing about firsthand advances in oncology.

In this context, finding cost-effective solutions that offer value for all parties involved in the day-to-day work of our Institution is a

constant necessity. Therefore, we are entering the final phase of introducing a new hospital management system, the implementation of which has, without a doubt, been one of the biggest challenges we faced in 2019.

With digital culture now transforming all spheres of life, a major advancement in education was achieved with the introduction of the Digital Teaching Center, which allows for additional flexible alternatives for the development of and access to educational content. We offered 12 courses, some 100% online and others hybrid, with over 75% adherence. We approved new development courses and began training with the use of simulators and virtual reality resources. For our *stricto sensu* students, the graduate education section has developed a professional masters (already submitted to the Coordination of Higher-level Personal Development, Capes). The goal of the degree is to develop scientific reasoning in professionals from different areas and generate innovations for society with a focus on health. We graduated 122 doctors and specialist physicians, including 80 medical residents, 28 multidisciplinary participants, and 14 continuing education participants. A total of 80 graduate students obtained masters and doctorate degrees, 22 students completed the PIBIC (Institutional Fellowship Program for Undergraduate Research), and 8 doctors completed the postdoctoral program.

Research is connected to all spheres of the Institution through incentives for scientific production, case discussion, and the mapping and introduction of new procedures, treatments and technologies. Investment in knowledge generation reached R$27 million, which was allocated to infrastructure, human resources and research reagents (consumables). Of this investment, nearly R$20 million was invested directly by the A.C.Camargo and R$7 million was gathered by the agency from national and international sources. There were 221 articles published in indexed international scientific journals and 174 research projects were concluded.

In addition, the research division formed 19 national and 35 international agreements, some of which already started in 2019. We have maintained cooperation agreements with foreign centers, such as Institut Curie in France, a leading cancer research institution in Europe with a focus on radiation therapy. We also signed a collaboration agreement with the Princess Margaret Cancer Centre, which provides the main cancer reference site for Canada. Our institution remains the headquarters for the National Institute for Science and Technology in Oncogenomics and Therapeutic Innovation (*Instituto Nacional de Ciência e Tecnologia em Oncogenômica e Inovação Terapêutica*, INCITO-INOTE), which brings together various national and international institutions for the development of scientific research, professional training, and the dissemination of knowledge to the public. INCITO-INOTE has support from the Brazilian National Council for Scientific and Technological Development (CNPq), the Coordination for the Improvement of Higher Education Personnel (CAPES), and

the State of São Paulo Research Support Foundation (FAPESP).

One of the most significant developments in the areas of education and research was the establishment of the Antônio Prudente Foundation's Endowment Fund for Education and Research, which reflects our commitment to sustainable investment in the production and dissemination of medical and scientific knowledge. The fund's objective is to lend support to research and education through contributions from the Institution's own resources and through third-party donations. The development of these initiatives will make possible the incremental and innovative transfer of meritorious knowledge related to cancer treatments.

We started 2020 with unimaginable challenges in healthcare due to the emergence of a pandemic caused by the new coronavirus, which causes Covid-19. We initiated daily monitoring of the impact on our staff, patients, visitors and providers; we acted in an agile way to mitigate all risks and to meet the demands of patients who contracted this infectious complex adequately. Healthcare is indubitably one of the world's most pandemic-impacted industries and patients with cancer have elevated susceptibility to infection and are at heightened risk of serious clinical outcomes. We are positive that we will be stronger after this challenge, reifying A.C.Camargo Cancer Center as a safe environment for patients and staff. We are continuing with our plans focused on the Institution's sustainability and mission to fight against cancer, patient by patient, in accordance with our values. We would like to honor our staff, who have worked every day through this challenge.

We would like to thank the volunteers and members of our Board of Trustees for all their contributions; our clinical staff for the support they have given to this administration; and our patients, their families, and society as a whole for the confidence placed in our work and for the privilege of being able to continue to make this history together.

José Ermírio de Moraes Neto
Chairman of the Board of Trustees

José Hermílio Curado
Institutional President of the Board of Trustees

José Marcelo Amatuzzi de Oliveira
Chief Executive Officer

Vilma Regina Martins
Chief Research Officer

José Humberto Fregnani
Chief Education Officer

ADVANCES IN **RESEARCH AND EDUCATION**

2019 IN NUMBERS

Introduction Introduction of the Digital Teaching Center

199 students enrolled at graduate level

80 new MAs and doctors

71 members of the education staff

191 participants in the Training of Teachers and Preceptors

221 articles published in indexed scientific periodicals

24 FAPESP grants, directly tied to the advisor/supervisor

R$ **27 million** invested in research

225 new research projects started

179 projects concluded

455 statistical consultations conducted

834 patients with samples collected by the Biobank

ABOUT THE INSTITUTION

The A.C.Camargo Cancer Center is a private non-profit institution based in São Paulo that serves as a reference center for cancer diagnosis, treatment, education and research. Active since 1953, it offers cancer services to private and National Health System.

Throughout a patient's journey with us, the Institution's goals are to provide integrated highly complex care safely and with a humanized attitude. The healthcare team inclusive of doctors, teachers, and scientists work together in caring for each patient and in the development of research and education. In this way, our knowledge dissemination has achieved international levels that have helped position the Institute as a global reference point in the fight against cancer. A fundamental part of our research structure, the International Cancer Research Center (Centro Internacional de Pesquisa, CIPE) working alongside clinical researchers in patient care strengthen our cancer treatment activities, leading to higher indexes for cure and survival. Investment in scientific research and innovation has been fundamental to this process.

In terms of the Institution's integrated approach, research and education are a priorities in our practice. Research and education activities are carried out mainly through basic, translational, and clinical research and, *stricto sensu*, through the graduate program in oncology.

THE CANCER CENTER'S **PERFORMANCE CYCLE**

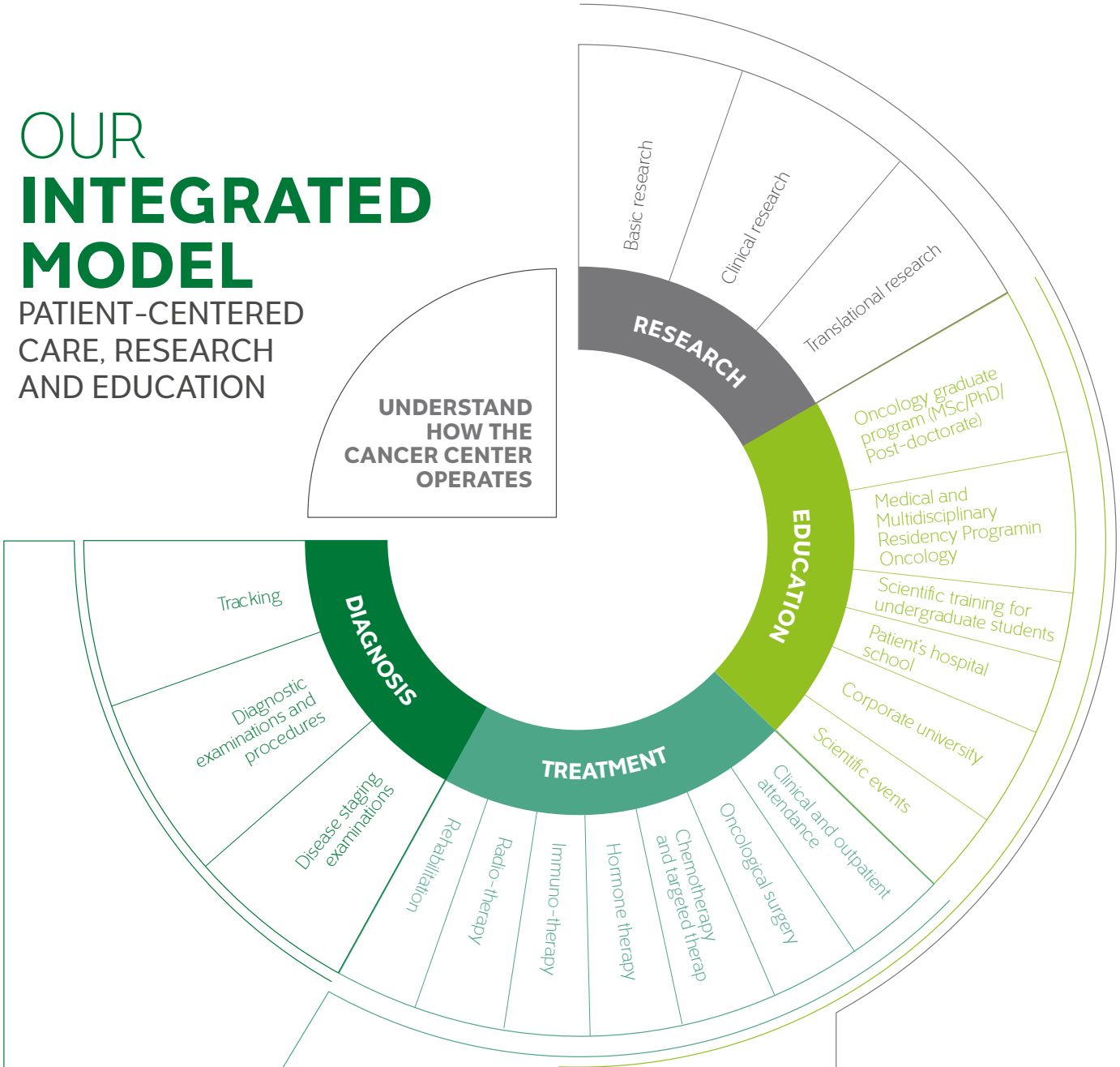
A.C.Camargo performs the functions of translating the cancer center model into effective responses to oncology challenges. Through this model of practice, our specialist staff, integrated into multidisciplinary teams, act together to offer patients the best possible services over the various steps of their treatment, including precise disease diagnosis and staging.

In such an environment, research and education play a fundamental role in the generation and application of scientific knowledge while staff training is the basis for advancement in combating cancer. Whether through day-to-day practice, complex activities, or technological development, it is through our scientific activity that we will be able to cross into new frontiers.

Education activity involving specialist training and graduate masters and doctoral programs, focusing on student-centered training in service, practical apprenticeship, and the development and application of scientific method, is an essential pillar of a cancer center.

OUR **INTEGRATED MODEL**

PATIENT-CENTERED CARE, RESEARCH AND EDUCATION



DIAGNOSIS

On arrival at A.C.Camargo with suspected cancer, either from the private or public healthcare systems, the patient is received by a multidisciplinary team and undergoes a battery of highly accurate exams in order to obtain a clear diagnosis and a good understanding of the stage of the disease.

TREATMENT

The institution's care practices are based on clinical and scientific evidence. They consist of medical and multidisciplinary specialist monitoring, consultations, surgeries, outpatient and inpatient procedures and treatments, with a focus on the recovery of each patient's health and well-being.

EDUCATION

Education at A.C.Camargo is centered on the formation, both in academic and practical terms, of researchers and clinical staff who are highly qualified in oncology, thereby contributing to meeting the demands of the labor market, academy and the institution itself. As a reference in the area of oncology, the institution generates and disseminates knowledge on cancer, both in Brazil and internationally.

SCIENTIFIC RESEARCH

The study of cancer and its complexities are the focus of clinical, molecular, genetic, genomic and immunological research. Together, these disciplines, seek to find treatments that are more efficient and cost-effective, and to unveil the disease's mechanisms. In this way, they aggregate knowledge to provide care for cancer patients on an individual basis. In our collegiate discussion forums, which bring together doctors, scientists and the multidisciplinary team, the analysis of complex patient cases can provide information for new research that will generate more effective therapeutic approaches.

MORE INFORMATION

More information on A.C.Camargo's history can be found at: https://accamargo.org.br/cancer-center/nossa-historia

2020–2025 **STRATEGY**

In 2019, we designed a new five-year strategic plan. In the next cycle, A.C.Camargo's actions will be regulated by structured strategic planning that will enable us to face the challenges and opportunities created by new technologies, healthcare access, economies of scale, changes to pay models and competitiveness. Structured around six pillars, the plan's priorities include, among other priorities, the consolidation of the cancer center model guided by integration of the areas of care, education and research. This approach will intensify the Institution's strengths toward the development and dissemination of cancer knowledge.

Consolidate the *cancer center* model by integrating patient care, education and research, in order to offer humanized and coordinated care, patient by patient, based on scientific evidence and best practices.

Increase competitiveness through the adoption of innovative technologies and the more efficient use of data, to provide patients with a better treatment experience and improved quality of life.

Search for new solutions to increase the survival rate and quality of life of patients, by incorporating new technologies in treatment with the lowest possible cost, ensuring competitiveness and increased acess.

Increase the number of patients under treatment both directly and indirectly, through partnerships, by means of sustainable projects and practices, establishing long-term relationships.

Continuously improve the efficiency of the institution's critical processes, ensuring the level of quality and speed required by the market.

Improve the patient's pathway experience, by staff development and training, ensuring that the patientcentered focus permeates all our decisions.

RESEARCH **AT A.C.CAMARGO**

Through research, we develop new therapies and technologies, thus increasing the effectiveness of treatments and improving the quality of life and survival of our patients. For this purpose, A.C.Camargo has an International Cancer Research Center (CIPE), which is a space dedicated to the development of scientific knowledge with the latest generation laboratories for scientists to work alongside clinical healthcare team members.

A.C.Camargo has national and international partners interested in making significant advances in cancer therapeutics through their research, particularly in the following areas: genetics and genomics, epidemiology, immune-oncology, new medications, new surgical and diagnostic techniques, big data, artificial intelligence in image processing and analysis, bioengineering and material sciences. The best way to spread the knowledge accumulated in these areas is publishing articles in scientific journals and deploying this knowledge to improve clinical practices. In 2019, the Institution's clinical and scientific staff published a total of 221 papers in indexed international journals.

Dr. Ludmilla Thomé Domingos Chinen, researcher, analyzing circulating tumor cells

INVESTIGATION AXES

BASIC RESEARCH: through analyses of tumor tissues, cells and microorganisms, scientists are seeking to elucidate the mechanisms and factors relating to the appearance, progression and spread (metastasis) of tumors. The process involves the mapping of targets for therapy and the identification of biomarkers for diagnosis, prognosis and treatment response.

39 articles published

TRANSLATIONAL RESEARCH: the meeting point between theory and practice, this axis leads to molecular knowledge of the mechanisms of tumor processes, yields results from patient studies and biological material collected for clinical practice and vice versa. Keeping in mind its expertise and relevance to Brazil, in this category of research, the Institution prioritizes studies focused on head and neck carcinomas, stomach and kidney tumors, sarcomas, breast, colorectal, lung and rare and hereditary tumors.

34 articles published

CLINICAL RESEARCH: this area involves the development of studies intended to improve clinical practice inclusive of diagnosis, prognosis and risk factor knowledge, as well as the development of new technologies and medications. It also includes partnerships with the pharmaceutical and equipment industries to meet the aim of promoting improvement across the course of the patient's cancer journey.

148 articles published

DISCUSSION FORUMS

Oncological Radar: mechanism for monitoring oncology trends that maps questions of technology, innovation, market and healthcare with the participation of doctors and scientists.

Research, Patient Care and Education Forum: promotes integration of the cancer center model with discussion and alignment of strategy for the three axes of action.

Research Boards: study meetings among scientists and doctors from different areas to discuss relevant themes as well as those little explored by basic, translational and clinical oncology research. The meetings facilitate the structuring of new ideas, thereby supporting the organization of scientific projects. The results obtained contribute to the generation of knowledge, which translates into clinical applications and has direct benefits for cancer patients and society.

Tumor Boards: multidisciplinary meetings to discuss the most effective therapeutic conduct for complex cases that fall outside of standard clinical protocols. The team also gives second opinions, updates conduct for clinical and educational protocols, and generates questions for the areas of basic and clinical research.

INTEGRATION OF RESEARCH WITH **REFERENCE CENTERS**

Key to the consolidation of the cancer center model, the reference centers (RCs) were expanded in 2019. By organizing care around the primary anatomical site of the tumor or specific characteristics (pediatric tumors and sarcomas), the course of treatment and multidisciplinary care becomes integrated and aligned with individual patients' needs.

The development of research and education based on each RC allows the entire staff involved in this activity to learn about and participate in the design and implementation of scientific research, development of clinical diagnostic protocols, treatment and rehabilitation with cost effectiveness, thus facilitating the search for better cure indexes and, ultimately, enabling the achievement of improved quality of life.

INDICATORS OF RESEARCH PRODUCTIVITY

RESEARCH DATA PLATFORM

- **145 new databanks** created on the REDCap platform during the year 2019, raising the number accumulated to 193
- **455 statistical** consultation cases

PRODUCTIVITY AND TECHNOLOGY TRANSFER

- **395 active projects** on the acProjects system
- **225 new projects** started
- **179 projects concluded**

PATIENT PARTICIPATION IN RESEARCH

- **1,255 free consent forms** applied by the team of research nurses during the month of September
- **1887 samples of biological material collected** by research nurses.

INVESTIMENTS AND **SUPPORT OF RESEARCH**

To expand our results in knowledge production, the Institution considers it strategic to capture resources and investments. In 2019, R$27 million was invested in infrastructure, human resources and reagents (consumables) in the research division.

With respect to the volume of resources captured, R$7.1 million (26.5%) came from national research support agencies, such as FAPESP and CNPq, and from Brazilian Health Ministry programs, such as PRONON and PRONAS. Added to these were international resources, such as those coming from the World Health Organization (IARC - International Agency for Research on Cancer) and the International Atomic Energy Agency.

RESEARCH INVESTMENT (R$)	**(R$)**
OUR OWN RESOURCES	19,930,103
NATIONAL INSITUTIONS	7,121,291
INTERNATIONAL INSTITUTIONS	6,947
TOTAL	**27,058,341**

RESEARCH SUPPORT – RESOURCES FROM INTERNATIONAL SOURCES 2019 (R$ THOUSAND)	**2019 (R$ THOUSAND)**
INTERNATIONAL AGENCY FOR RESEARCH ON CANCER – IARC/INTERCHANGE (WHO)	1,110
INTERNATIONAL ATOMIC ENERGY AGENCY - IAEA	5,837
TOTAL	6,947

RESEARCH SUPPORT – RESOURCES FROM NATIONAL SOURCES	**(R$)**
FAPESP*	2,612,295
CNPQ*	460,720
CONDUCT ADJUSTMENT AGREEMENT (TAC) – LABOR PUBLIC MINISTRY	186,223
PRONON/ BRAZILIAN HEALTH MINISTRY – TUMOR BANK FOR RESEARCH IN THE TREATMENT, PREVENTION AND EARLY DIAGNOSIS OF CANCER	3,197,579
PRONON/ BRAZILIAN HEALTH MINISTRY – PERSONALIZED MEDICINE	299,707
PRONON/ BRAZILIAN HEALTH MINISTRY – STUDY OF THE MICROBIAL PROFILE OF TUMORS IN HUMANS	243,575
PRONAS/ BRAZILIAN HEALTH MINISTRY – PROGRAM FOR THE REHABILITATION OF PATIENTS IN TREATMENT FOR CANCER	114,367
OTHER**	6,825
TOTAL	7,121,291

* Value represents the sum of graduate fellowships and research assistants.
** Studies initiated by the investigator.

Dr. Marina De Brot Andrade, pathologist, looking at samples stored in the Biobank

SPONSORED CLINICAL RESEARCH

Sponsored clinical research is responsible for developing new, safer and more effective medications in accordance with technoscientific and highly rigid ethical precepts. Therefore, it is a fundamental part of a complete and innovative cancer center. After the laboratory study phase, new medications are advanced to phase I studies, which are performed on a small number of patients to evaluate treatment safety. In phase II studies, treatment effectiveness is assessed in a slightly larger pool of patients. In phase III studies, new treatments are compared with the current standard treatment; they involve a large number of patients and treatment centers in different countries. In some cases, there may be phase IV studies, which are conducted after a new treatment has been approved by the relevant regulatory bodies (in Brazil, Anvisa – the Brazilian Health Regulatory Agency) to evaluate less common side effects and the long-term impact on the population. There is also a trial program for new medications that have already been approved abroad but are awaiting Anvisa approval.

Sponsored clinical studies to be initiated at A.C.Camargo are selected based on the Medical Coordinator for Clinical Studies analysis of proposals from the pharmaceutical industry or from the clinical staff. The decision to participate in a study is based on its scientific relevance, safety and potential contributions to A.C.Camargo. In 2019, 53 phase II and III studies were in progress at the Institution (29 started in 2019), covering 17 different types of tumors.

Sponsored clinical studies ensure A.C.Camargo's innovation in partnership with the pharmaceutical industry and offer patients the possibility of participating in clinical protocols that are responsible for the advancement of science and capable of generating future clinical benefits, including increases in cancer survival and cure rates. There is also the gain in terms of the improvement of treatment and non-care-related processes that clinical research training brings to A.C.Camargo's entire clinical and scientific corps.

PHASES OF SPONSORED STUDIES

Phase 1. Involving a small number of patients, with the goal of evaluating treatment safety;

Phase 2. Involving a moderate number of participants, with the goal of measuring efficacy;

Phase 3. Vigorous comparison of the treatment under development to standard treatments in a large sample of patients from different countries;

Phase 4. Intended to detect low-frequency side effects and long-term impacts on the population*.

* This phase is performed only when necessary, such as in the case of studies that take place after the relevant regulatory bodies have approved the treatment.

SUPPORTED CLINICAL STUDIES BEING RUN AT A.C.CAMARGO BY TREATMENT PROTOCOL TYPE

TYPE OF TREATAMENT	CHEMOTHERAPY	IMMUNOTHERAPY	TARGETED THERAPY	CARE PROGRAM	OTHER*	TOTAL
STUDIES	1	20	14	16	2	53
NUMBER OF PATIENTS	16	43	60	147	40	306
NUMBER OF CONSULTATIONS	97	134	234	263	62	790

**Hormone therapy and pain.*

THE BIOBANK AS A REFERENCE STRUCTURE

Created in 1997, the A.C.Camargo's Biobank is one of the largest in Latin America. With the participation of patients and volunteers from prevention programs, we have already collected, in total, more than 44.9 thousand samples of tumors, normal tissues and blood. This archive allows us to undertake research capable of enhancing knowledge about early diagnosis, diagnostic tools and treatment tools. Additionally, the Biobank allows us to study genetic modifications that might increase cancer risk, affect treatment response, or inform the development of new medications.

SAMPLES COLLECTED FOR THE BIOBANK/METRICS	QUANTITY
BLOOD SAMPLES	721
TISSUE COLLECTED AND FROZEN	1,658
RESEARCH PROJECTS USING SAMPLES STORED IN THE BIOBANK	28
Nº OF PATIENTS RECRUITED IN THE YEAR 2019	834
Nº OF DNA AND RNA EXTRACTIONS IN 2019	1,545
Nº OF SAMPLES PROCESSED IN 2019*	5,699
Nº OF CASES COLLECTED SINCE THE CREATION OF THE BIOBANK	44,966
Nº OF PATIENTS RECRUITED SINCE THE CREATION OF THE BIOBANK	41,493
Nº OF DNA AND RNA EXTRACTIONS ACCUMULATED SINCE 2004	26,143

**The number of samples processed is a metric, introduced in this reporting cycle, which reflects the volume of activity of the Biobank laboratory.*

EDUCATION AT **A.C.CAMARGO**

On the education front, we would like to emphasize A.C.Camargo's *Stricto Sensu* Graduate Program, which has a teaching staff made up of scientists who are active and recognized in oncology and a multidisciplinary team that works cooperatively toward the goal of transforming care activities into scientific knowledge. There are 67 teachers to look after 199 enrolled students.

Over the course of the year, we held 19 public seminars with speakers specializing in key areas, such as telemedicine and the cancer center's own model.

As to the events promoted during this period, we would like to highlight Next Frontiers to Cure Cancer, an international conference organized by A.C.Camargo to discuss major research advances and innovations in cancer treatment and diagnosis. Aimed at physicians, scientists and staff from different fields, such as nursing and physiotherapy, this conference is already considered a major event on Brazil's cancer agenda. In 2019, it involved 1,506 participants and 352 speakers, 38 of whom were international.

A.C.CAMARGO SEMINARS

THEME	SPEAKER
CANCER CENTER: INTEGRATION OF CARE, EDUCATION AND RESEARCH	Dr. Victor Piana de Andrade
A BREAST CANCER REFERENCE CENTER: CARE AND RESEARCH	Dr. Fabiana Baroni A. Makdissi
RESEARCH AT THE A.C.CAMARGO: ACTIVITIES AND PERSPECTIVES	Dr. Vilma Martins
CURRENT PUBLIC AND PRIVATE HEALTH SYSTEM AND ITS CHALLENGES	Dr. Gonzalo Vecina Neto, assistant professor at FSP/USP and teacher for the professional masters at EASP/FGV
GRADUATE EDUCATION IN MEDICINE IN BRAZIL: CONQUESTS, CHANGES, AND CHALLENGES	Dr. Luis Felipe Ribeiro Pinto, coordinator for the area of Medicine I at Capes and full professor at the National Cancer Institute (INCA)
TELEMEDICINE	Dr. Chao Lung Wen, associate professor at FMUSP and head of the division of Telemedicine.
PANORAMA OF THE GENOTYPES AND PHENOTYPES OF TYPE 2 MULTIPLE ENDOCRINE NEOPLASIA (MEN2) IN 554 PATIENTS WITH MEDULLARY THYROID CANCER: THE BRASMEN STUDY	Dr. Rui Monteiro de Barros Maciel – UNIFESP
NEXT FRONTIERS HIGHLIGHTS	Dr. José Humberto Fregnani
CLINICAL RESEARCH AT THE A.C.CAMARGO – PATHOLOGIC ANATOMY: RESEARCH AND TREATMENT	Dr. Antônio Geraldo do Nascimento
FUNDAMENTALS OF PLASMA AND PLASMA APPLICATIONS IN MEDICINE AND ONCOLOGY	Dr. Nilson Cristiano da Cruz
HEAD AND NECK CANCER RESEARCH	Dr. Luiz Paulo Kowalski
RADIOLOGY AND MEDICAL PHYSICS: RESEARCH AND TREATMENT	Dr. Antônio Cássio Assis Pellizzon
THE IMMUNOTHERAPY CENTER: RESEARCH AND TREATMENT	Dr. Milton José de Barros e Silva
RESEARCH ON KIDNEY TUMORS	Dr. Stênio Zequi
DOCTORAL PROJECT ON "THE MEDIA'S INFLUENCE ON THE DIAGNOSIS OF BREAST CANCER BY CLINICAL STAGE"	Dr. José de Moura Leite Netto
DOCTORAL PROJECT: "MIR-4728-3P AND HER2 BIOLOGY: STUDYING A POORLY CHARACTERIZED INTRONIC MESSAGE HIDDEN IN THE ERBB2 ONCOGENE"	Dr. Emilio Tarcitano
HEALTH APPLICATIONS OF NANOTECHNOLOGY: ADVANCES IN NANOMEDICINE AND NANOTOXICOLOGY	Dr. Valdeci Zucolotto – USP/São Carlos
CYTOPATHOLOGY AND RAPID EVALUATION: OPTIMIZING DIAGNOSIS	Dr. Mauro Tadeu Ajaj Saieg

STUDENTS GRADUATING IN 2019

MASTER

Adriano de Oliveira Beserra
Alessandra Marumi Emori Takahashi
Ana Carolina Cantelli Pereira
Ana Gabriela Silva de Lima
Ana Luiza de Souza Bezerra Lira
André Marcondes Braga Ribeiro
Bruno Hurtado Rodrigues
Camila de Moura Gatti
Cintia Maria da Silva Dutra
Conceição Hander de Lucena
Daniel Gaspar Gonçalves
Danielle Pereira Nascimento
Edla Karina Cabral de Oliveira
Francieli Batista Haus da Costa Pereira
Graziela Parnoff Pereira Baladão
Jeane Alves da Silva
Jéssica Piro Barragam
José Eduardo Núnez Rodriguez
Juliana Brandão Folador Morellato
Juvaniêr Romão Cruz
Leandro Spinelli
Marcela de Araújo Fagundes
Marcos Vinicius Odorissio Ferrari
Maryane Caroline de Toledo
Matheus Henrique Alves de Lima
Melissa Gonçalves da Silva
Patricia Alves de Senna
Paula do Amaral Costa Ribeiro
Penelope Sanchez Teixeira
Sílvia Regina Negri
Thalissa Maniaes
Victor Hugo Fonseca de Jesus
Vinicius Gonçalves de Almeida

PHD

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Camila Silva Bôaventura
Carlos Cesar de Oliveira Ramos
Caroline Moraes Beltrâmi
Eloisa Helena Ribeiro Olivieri
Emilio Tarcitano
Emne Ali Abdallah
Erika Regina Matheus Malentacchi
Fabio Fernando Eloi Pinto
Fábio Medeiros de Azevedo
Felipe da Silva Marinho
Felipe D'almeida Costa
Felipe Dubourcq de Barros
Fernanda Berti Rocha Mendes
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Gilcy Raymundo Damm
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Helano Carioca Freitas
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Jaqueline Munaretto Timm Baiocchi
José de Moura Leite Netto
Josualdo Justino Alves Junior
Julia Bette Homem de Mello
Kivvi Duarte de Mello Nakamura
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Luiz Renato Montez Guidoni
Luiza Taciana Rodrigues de Moura
Marcelo Cavicchioli
Marcelo Ramos Tejo Salgado
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Rita de Cássia Freitas Bandeira
Rogerio Luiz dos Santos
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Tatiane Ramos Basso
Tercia Jovino Neves Santos
Thiago Bueno de Oliveira
Ulisses Ribaldo Nicolau
Vandré Cabral Gomes Carneiro

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Maria Angélica Ferreira Dias
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Vilma Regina Martins
Vladmir Claudio Cordeiro de Lima
Walter Henriques da Costa
Wilson Luiz da Costa Junior

FIELDS TAUGHT BY THE GRADUATE PROGRAM

FIELD	TEACHER RESPONSIBLE
A.C.Camargo Uro-Onco Journal Club	Dr. Stênio de Cássio Zequi and Dr. Walter Henriques da Costa
Therapeutic Updates Based on Targeted Therapy and Translational Medicine	Dr. Aldo Lourenço Abbade Dettino; Dr.Celso Abdon Lopes de Mello; Dr. Ludmilla Thomé Domingos Chinen and Dr. Vladmir Cláudio Cordeiro de Lima
Bases of Molecular and Cellular Biology	Dr. Glaucia Hajj, Dr. Tiago Góss and Dr. Vilma Martins
Basic Research Seminar Series I	Dr. Martin Roffé
Basic Research Seminar Series II	Dr. Martin Roffé
Bioethics	Dr. Glaucia Hajj, Dr Tiago Góss and Dr. Samuel Aguiar Jr.
Biocomputing Applied to the Study of Cancer Genomics	Dr. Israel Tojal da Silva and Dr. Rodrigo Drummond
Cancer System Biology	Dr. Fabio de Albuquerque Marchi
Breast Cancer	Dr. Fabiana Baroni Alves Makdissi and Dr. Almir Galvão Vieira Bitencourt
Cancer Surgery	Dr. Ademar Lopes and Dr. Hirofumi Iyeyasu
Cancer Pain	Dr. José Oswaldo de Oliveira Junior and Dr. Fabio Henrique de Gobbi Porto
Descriptive Epidemiology of Cancer	Dr. Maria Paula Curado
Statistics I	Dr. Vinicius Fernando Casalvara
Statistics II	Dr. Vinicius Fernando Casalvara
Control Study in Cancer	Dr. Maria Paula Curado
Basics of Radio-oncology	Dr. Antônio Cássio Assis Pellizzon
Research Basics	Dr. Rachel Simões Riechelmann
Cancer Imaging 1: The Basics	Dr. Marcos Duarte Guimarães, Dr. Eduardo Nóbrega Pereira Lima and Dr. Chiang Jeng Tyng
Cancer Imaging 2: Advanced Methods	Dr. Rubens Chojniak; Dr. Almir Galvão Vieira Bitencourt and Dr. Paula Nicole Vieira Barbosa
Immune Epigenetics of Cancer	Dr. Tiago da Silva Medina
Immunotherapy	Dr. Tiago da Silva Medina and Dr. Kenneth John Gollob
Scientific Research Methods	Dr. Maria Paula Curado, Dr. Antonio Paulo Nassar and Dr. Wilson da Costa Junior
Microbiome and Immune Regulation in Cancer	Dr. Diana Noronha Nunes and Dr. Emmanuel Dias-Neto
Oncourology	Dr. Stênio de Cássio Zequi
Oncogenetics	Dr. Maria Nirvana da Cruz Formiga and Dr. Giovana Tardin Torrezan
Head and Neck Oncology	Dr. Luiz Paulo Kowalski, Dr. João Gonçalves Filho and Dr. José Guilherme Vartanian
Personalized Oncology: Bases and Applications of Genomic Tests	Dr. Dirce Maria Carraro and Dr. Giovana Tardin Torrezan
Tumor Pathology	Dr. Marina De Brot, Dr.Louise De Brot and Dr. Mauro Saieg
Research and Education Platforms	Dr. Rubens Chojniak
Scientific Communication In English	Dr. Victor Piana de Andrade; Dr. Tiago Góss dos Santos and Dr. Giovana Tardin Torrezan
A.C.Camargo Seminars	Dr. Rubens Chojniak

HIGHLIGHTS: **SCIENTIFIC ARTICLES, DISSERTATIONS AND THESES**

SCIENTIFIC ARTICLES

TREATMENT – NEW DRUGS, SURGICAL APPROACHES AND RISK PREDICTION TOOLS

New molecule for treating head and neck tumors benefits patients with deglutination difficulties

Patients with head and neck tumors often have difficulty swallowing and do not adhere well to oral medication. A second-line treatment study with Afatinib (Giotrif), a small inhibitor molecule of ErbB kinase proteins, showed bioactivity and increased the survival of patients with squamous cell head and neck tumors compared to the standard treatment. An analysis of subgroups of these patients showed high use adherence to the medication, which was safe and effective. Observed side effects were similar whether it was administered orally or by probe. Thus, it was concluded that the medication can be used in an efficient way without compromising the treatment of patients who have difficulty swallowing, which is of great benefit. Access here.

New medication for lung tumor treatment shows positive effects in a real-world study

A real-world study examined the effectiveness of osimertinib against non-small cell lung cancer. The medicine is a third-generation irreversible epidermal growth factor receptor (EGFR) inhibitor targeting the T790M mutation. The initial primary and secondary findings obtained by evaluating more than 3,000 patients showed effectiveness in terms of increased survival, longer survival free from progression, and a longer treatment discontinuation period. Treatment side effects, including interstitial pulmonary disease and pneumonitis, were identified in 1% of the patients. The data obtained are similar to those found in the initial clinical trial, thus supporting osimertinib use in patients with tumors carrying the EGFR T790M mutation. There are still patients continuing to participate in this clinical study at our center and benefitting from this medication. Acess here.

Dr. Ulisses Nicolau

Dr. Helano Freitas

Effectiveness of everolimus and sunitinib in the treatment of pancreatic neuroendocrine tumors with the NEN gene mutation

Neuroendocrine tumors can affect any organ of the body and are considered rare given that they make up less than 1% of all cancer cases. This rareness has affected whether robust studies of new therapeutic approaches are conducted. Approximately 10% of these tumors are associated with hereditary syndromes through mutations in the NEN1 and VHL genes; another group of these tumors is sporadic. A retrospective, multicenter study on pancreatic neuroendocrine tumors was conducted to evaluate responses to treatment with everolimus and sunitinib, which inhibit the cell pathways modulated by the NEN and VHL gene products. The results obtained suggest that everolimus offers a more prolonged control of tumors with germline NEN1 and VHL mutations versus that seen in sporadic tumors. Sunitinib's effects could not be evaluated due to the small number of patients in this retrospective group. Notwithstanding, clinical studies need to be conducted to confirm the effects these drugs have on the treatment of these rare tumors with few treatment options. Acess here.

Dr. Rachel Riechelmann, Dr. Milton Barros and Dr. Maria Nirvana Formiga

Perineural invasion allows for the identification of greater risk of recurrence in postoperative patients who had early-stage gastric tumors and supports adjuvant treatment

Patients with stage 1 gastric cancer have an excellent prognosis after surgical treatment. However, some fall sick again, particularly those who are in stage 1B. This study, performed using tracking data from 185 patients, showed that the presence of perineural invasion is associated with an increased likelihood of tumor recurrence. In these cases, the use of adjuvant chemotherapy should be considered. Additionally, many patients with initial gastric tumors die of causes not related to this tumor. Therefore, greater effort should be placed on the control of comorbidities and on finding other primary tumors in this population. This approach would certainly benefit patients, who would gain a greater likelihood of controlling the disease. Acess here.

Dr. Victor Hugo F. de Jesus

Use of nomograms as a tool to predict recurrence risk in patients with cutaneous melanomas

Nomograms are graphic representations of statistical study results that provide highly objective information to users. This type of tool is very common in oncology. Two consecutive studies allowed nomograms to be explored in relation to cutaneous melanomas. The first one addressed patients with a negative biopsy of the sentinel lymph node presenting with a heterogenous outcome; there was no stratification of patients for risk and adjuvant treatment data was scarce. Based on this unresolved question, a nomogram was generated using an institutional cohort of more than 1,200 participants. It identified those with negative sentinel lymph nodes and a high risk of disease recurrence. This tool makes it possible to establish patient follow-up and to request exams based on individual risk - that is, individualized evaluation that results in better practices. The second study validated the institutional data in a cohort of Dutch patients. The nomograms are available on the institution's website; and the more they are used, the easier it will be to incorporate them into clinical practice and to establish changes to treatment. Acess here and here.

Dr. Eduardo Bertolli

Individualized treatment for preventing postoperative complications in patients treated for gastric tumors

Stomach cancer affects more than a million people worldwide every year. The majority of these patients are diagnosed with an advanced-stage tumor and treated surgically. Postoperative complications can affect the long-term outcomes of treatment. A study involving data from 1,223 patients was conducted to identify predictors of postoperative morbidity, including older age, chronic obstructive pulmonary disorder, heart disease, chronic liver disease, pancreatic resection, and duration of surgery. Knowledge of these risk factors allows an individualized treatment plan to be developed for each patient, avoiding postoperative complications and improving patient safety. Acess here.

Dr. Felipe Coimbra

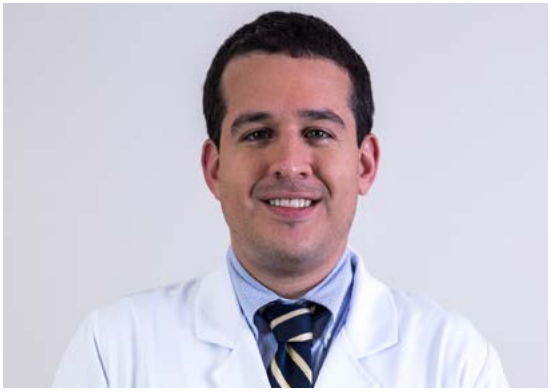
Improvement in the quality of radical prostatectomy through robotic surgery

Prostate tumors are the most common cancer incidents in the male population; and resection surgery is the most commonly used therapeutic approach to treating them. This study was conducted to report institutional experience with 1,088 patients with prostate cancer who underwent prostatectomy with innovations in the traditional technique of robotic surgery. The new robotic surgery approach contrasts with the traditional one in the following ways: nerve fiber-rich prostate tissues are preserved; high-cost imported surgical clips are not used; and the surgery is conducted through the pelvis, outside of the abdominal cavity. Oncological and urinary continence outcomes were similar to those of the traditional robotic technique. The patients operated on with this new technique had greater preservation of sexual potency (75.1% new vs. 53.5% traditional) and had substantially faster sexual function recovery (9.4 months new vs. 16.3 months traditional). However, it must be noted that the technique is contraindicated in cases of locally advanced tumors. This study showed that the new robotic technique for prostatectomy is safe and yields clear benefits to patients. Acess here.

Dr. Stenio Zequi

Radiation therapy approaches after breast cancer surgery bring excellent therapeutic results, reduce side effects, and reduce the treatment period

Conservative treatment for breast cancer was one of the most successful oncological advances of the 20th century. Postoperative radiation therapy after conservative surgery increases local control and global survival in breast cancer patients. However, treatment with conventional fractionation can be challenging both for patients and healthcare systems. Therefore, there have been various attempts to reduce treatment durations, especially with radiation. Currently, many studies note that the use of partial irradiation of the breast and various intraoperative radiation treatment techniques are clinically available. Apposite selection criteria for patients can enable excellent local control to be achieved (98.6% in our experience). Notable advantages of this form of radiation therapy are reduced skin reactions and greater patient comfort owing to the elimination of daily trips to hospitals or clinics for radiation treatment programs that would otherwise last three or more weeks. Furthermore, this approach may reduce the risk of adverse cardiovascular events, which should stimulate greater use of this treatment method in light of such direct benefits to the patient. Acess here.



Dr. Guilherme Gondim

SCIENTIFIC ARTICLES

MORE PRECISE DIAGNOSES

Breast magnetic resonance imaging (MRI) has a high level of sensitivity for diagnosing and evaluating responses to treatment for breast cancer

Breast cancer is a heterogenous disease with different forms of presentation, prognoses, and treatment options. Two studies showed that among the imaging options available, breast MRI provides the greatest sensitivity for diagnosing breast cancer together with precision in evaluating tumor heterogeneity and treatment response. The first study demonstrated that the way the tumor presents on MRI is related to prognosis, especially in young patients with breast cancer. The findings can contribute to better planning of patient treatment and follow-up. The second study, in turn, demonstrated that the MRI can also predict treatment responses as early as the end of the first cycle of chemotherapy, making more personalized management possible and allowing for toxic interventions that are not achieving an adequate response to be modified early on. Acess here.

Thyroid hormone levels in cell lavage increase sensitivity for detection of thyroid tumor recurrence

In patients with thyroid cancer, recurrence near the surgical site is common. That is, tumor cells often re-grow in the area where the thyroid gland previously was. To identify the presence of new malignant lesions, an ultrasound should be performed and followed up with a fine needle biopsy. In some cases, malignancy of remaining cells is uncertain. This study examined the utility of subjecting the material from the lavage of the biopsy needle to an assay for thyroglobulin, a hormone produced by the thyroid. The findings show that measuring thyroglobulin levels is useful and increases the sensitivity and the chance of finding remaining tumor cells in patients previously operated on for thyroid cancer. Therefore, continuous use of this approach enables enhanced monitoring of thyroid cancer patients. Acess here.

Dr. Almir Bitencourt

Dr. Mauro A. Saieg

SCIENTIFIC ARTICLES

ONGOING IMPROVEMENTS IN CRITICAL CARE

Presence of certified intensive care doctors in the intensive care unit (ICU) leads to better practices and reduced time on mechanical ventilation for patients

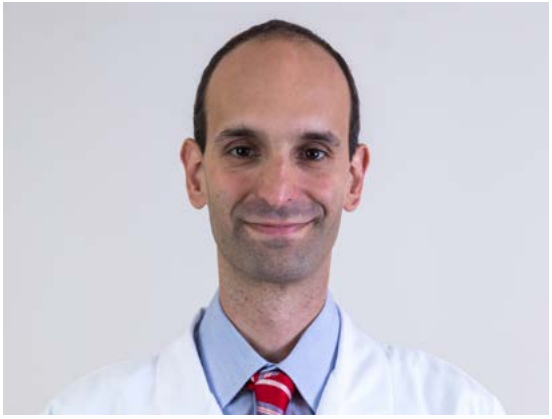
We know that strategies such as light sedation that keep a patient awake and with some sensation intact reduce the length of mechanical ventilation in ICU patients. However, the majority of ventilated patients are still kept deeply sedated (in an "induced coma"), especially during their first days on mechanical ventilation.

In a study conducted together with 118 ICUs across eight Brazilian institutions and involving 5,719 patients, we evaluated the organizational parameters that enabled better adherence to light sedation strategies in ICU patients on mechanical ventilation. The presence of certified intensive care doctors during the morning and afternoon shifts was shown to be associated with a 2.5 times higher level of adherence to this practice. This behavior by specialists has direct benefits on patient recovery. Acess here.

Protocols for hemodynamic monitoring and anesthesia improve postoperative results in patients with high levels of surgical risk

When under deep anesthesia, patients with high levels of surgical risk are subjected to hemodynamic monitoring. Establishing well-defined indications and objectives is fundamental to postoperative outcomes.

Monitoring protocols were established and evaluated based on comparative data from 596 patients, 313 before and 283 after the establishment of the protocol. The study demonstrated that implementing monitoring protocols with predefined clinical parameters during the anesthetic process improved postoperative outcomes. Compared to the before-protocol group, the after-protocol patients had half the rate of postoperative delirium, a third the rate of urinary tract infections, and a hospital stay duration that was reduced by about a day. In patients with large open abdominal surgeries, adoption of the protocol promoted a significant improvement in postoperative results. Access here.



Dr. Antônio Paulo Nassar Jr.

Dr. Mariana F. Lima

SCIENTIFIC ARTICLES

GENOMICS AND LIQUID BIOPSY IN TRACKING CANCER PATIENTS

Monitoring of gastric tumors through liquid biopsies of gastric juice during routine endoscopy

Between 1998 and 2000, A.C.Camargo was a pioneer in identifying cell-free tumor DNA in body fluids (i.e., liquid biopsy analysis). This approach allows for the identification of DNA fragments of tumor origin in body fluids, which offers a very-low-invasiveness means of monitoring a tumor during treatment and screening for recurrence.

The first study to demonstrate that cell-free DNA from stomach cancer cells can be found in the gastric cavity was completed, allowing evaluations to be performed during routine endoscopy, including the monitoring of treatment response. An important advantage to this approach is that gastric fluids allow the entire stomach cavity to be evaluated and not just visible lesions and material collected by biopsies. As a result, it is possible to identify gene mutations that can be targeted by known therapies, making it possible to adopt precision medicine strategies that have a positive impact on patient survival owing to appropriate treatment administration. Acess here.

Dr. Emmanuel Dias-Neto

Circulating tumor cells (CTCs) as liquid biopsy biomarkers of colorectal and gastric tumors

CTCs are released by tumors in body fluids, particularly in blood, and their detection, quantification, and molecular analysis allow for more appropriate therapies to be given in accordance with the particular tumor type. Two studies demonstrating the benefits of evaluating CTCs were conducted.

The first looked at colorectal carcinoma, one of the most common neoplasms in the Western world, where 30% of the cases are rectal tumors. In cases of locally advanced rectal tumors, the standard treatment is chemotherapy plus radiation followed by surgery. Evaluation of CTCs can occur at two points: before chemotherapy/radiation, defining whether the patients will benefit from the treatments despite their toxicity; or after chemo/radiation treatment, when it can be used together with imaging to evaluate treatment response. Total response to treatment can help to decide whether surgery, which is highly mutilating, should be performed. A similar approach can be used for gastric cancer, the third most lethal neoplasia in the world. In cases of local disease without metastasis, CTCs can contribute to treatment planning and prognosis.

The identification of the HER-2 protein in CTCs, unlike its presence in the primary tumor, was found to be directly associated with disease progression. This observation promoted the design of a phase II clinical trial in partnership with LIBBS Farmacêutica, which aims to define patient treatment based on CTC results. Acesse here and here.

Dr. Ludmilla Thomé Domingos Chinen

Lynch syndrome (LS) is poorly tracked in Latin America despite representing a high risk of colorectal tumors

A multicenter study with only nine (20%) Latin American countries developed protocols for the early detection of colorectal carcinoma. The group analyzed the genetic profile for LS, a hereditary cancer, in 2,685 suspected families and confirmed LS-associated variations ranging between 8%, in Uruguay, and 60%, in Peru. In Brazil, some rare LS-associated genetic variants were found to affect 15% of the families in the study group. These findings may affect the evaluation of patients and their family members at risk of LS given that 40-80% of the families in this study had not been identified despite meeting the clinical criteria for LS. The main challenges for Latin American countries are: to raise awareness of the population and health professionals about hereditary cancers; to improve training for both doctors and non-doctors in evaluating the genetic risk of cancer; to develop guidelines for evaluating risk; to track cancer and genetic testing for these conditions; and to implement genetic testing for patients in public and private healthcare systems. Acess here.

Dr. Dirce Maria Carraro and Dr. Maria Nirvana da Cruz Formiga

PHD DISSERTATIONS

***In situ* identification of lipidomic profiles for biphasic breast tumors through desorption electrospray ionization/mass spectrometry (DESI/MS)**

Monique Batista da Costa Lemos

Biphasic breast tumors are a heterogenous group of tumors that present two histological components: the epithelial and the stromal. They can be benign or malignant; some may recur or lead to metastasis. Their prognosis varies according to their histological classification, the presence of metastasis, and treatment adequacy. Nevertheless, sometimes it is difficult to differentiate them when there is an overlap in the histological characteristics used for diagnosis in anatomical pathology exams.

Searching for a new method to differentiate biphasic breast tumors from each other, aside from the usual anatomic pathology exam, we analyzed these tumors using an analytical chemical technique of environmental ionization with mass spectrometry known as DESI/MSI. Frozen slide-mounted samples were submitted to DESI/MSI analysis, which generated mass spectrums and chemical images. Statistical analysis was performed using the Wilcoxon-Mann-Whitney test. DESI/MSI chemical image analysis showed that it is possible to differentiate biphasic breast tumors. The future use of this technique in routine diagnosis could be promising, especially given its quick execution time and high accuracy.

Acess here.

Identification of CTCs and other blood components in patients with localized colon cancer

Emne Ali Abdallah

Early detection of colon cancer leads to high rates of cure. However, some patients have local recurrence and distant metastases that require complex treatment approaches. Unfortunately, the markers normally used and collected in blood tests do not yield precise information. Therefore, CTCs, which are cells released by the tumor during its development and progression, are an easy-access and important monitoring tool for these patients.

Blood samples from patients with localized colon cancer were analyzed for CTCs and the following other informative blood components: CD3-expressing T lymphocytes, which induce immune responses; regulatory T lymphocytes, which repress immune responses; and platelets, which are responsible for coagulation and clot formation. Blood samples were collected at three time points: pre-surgery; pre-adjuvant (after surgery, before chemotherapy), and six months after the final treatment. CTCs were isolated in ISET® equipment. Molecules related to treatment resistance, including ERCC1 (platinum resistance marker) and beta-galactosidase (general resistance marker) were evaluated in the CTCs of 69 patients (18 with stage I disease, 15 with stage II disease, and 36 with stage III disease). The CTC detection rate for the first, second, and third samples were 94.2%, 94.6% (pre-adjuvant), and 100%, respectively. A lower recurrence-free survival was found to be related to ERCC1 presence, which correlated directly with CTC and regulatory T lymphocyte counts, as well as to a high platelet-lymphocyte ratio. These data show that CTCs were found in high rates in patients with locally advanced colon cancer and that their presence correlated with immune-response inhibition and thus likely resistance to the proposed treatment scheme.

Acess here.

Phase II randomized and controlled clinical trial to evaluate the non-inferiority of extrafascial hysterectomy for the treatment of stage IA2 and stage IB1 cervical cancer (lesion ≤2 cm)

Vandré Cabral Gomes Carneiro

Cervical cancer is treated surgically. Radical resection with parametrectomy increases the treatment's morbidity, perhaps unnecessarily in patients with early-stage disease. Therefore, this study's objective was to compare the safety and efficacy of extrafascial hysterectomy versus modified radical hysterectomy in patients with stages IA2–IB1 cervical cancer (lesion ≤ 2 cm). Both operations were performed with bilateral pelvic lymphadenectomy

In a 1:1 proportion, 42 patients who were candidates for elective surgical treatment with a curative intent via extrafascial hysterectomy or modified radical hysterectomy, were randomized between May 2015 and April 2018; 40 of them being evaluated. Quality of life data were collected with the EORTC QLQ-30 questionnaire. Clinical and pathological characteristics were assessed prospectively.

Extrafascial hysterectomy was found to have low morbidity and was proven safe for the treatment of patients with early-stage cervical cancer. It did not appear to be inferior to modified radical hysterectomy with parametrectomy perhaps, which thus appears to be potentially unnecessary in this subpopulation. Data analysis of the primary outcome, after a longer follow-up, is anticipated before final conclusions are made.

Acesse aqui.

Use of 18FDG-PET-CT (2-[18F]-fluoro-2-deoxy-D-glucose positron emission tomography/computed tomography) to predict the effectiveness of treatments in terms of locoregional control and survival in patients with epidermoid carcinoma of the head and neck

Ulisses Ribaldo Nicolau

Treatment of oropharyngeal epidermoid carcinoma (EC) is based on disease extent as defined by primary tumor characteristics, regional lymph node involvement, and the presence of distant metastasis in accordance with the TNM (tumor-node-metastasis) rubric. Use of chemotherapy with radiation in neoadjuvant and concomitant modes is an established alternative for EC in patients diagnosed with advanced locoregional clinical stage III or IV disease without metastasis (i.e., M0).

A retrospective analysis of 75 patients diagnosed with and treated for stage III or IV (M0) oropharyngeal EC at A.C.Camargo between 1995 and 2010 with the combination of chemotherapy and radiation was conducted. Sociodemographic and clinical variables were accounted for. The potential prognostic role of cell cycle regulatory proteins associated with infection and carcinogenesis by human papilloma virus, namely the viral proteins p16 and p53, were evaluated by immunohistochemistry. Treatment response rates and survival rates were high. The variables found to be significant predictors of prognosis were primary tumor extent, tobacco use, alcohol use, and obtaining complete response.

Acess here.

MASTERS THESES

Validation of the instrument Lymphedema Functioning, Disability and Health Questionnaire for Lower Limb Lymphedema (LLL) with optoelectronic volumetry in patients with secondary lymphedema from cancer treatment

Jaqueline Munaretto Timm Baiocchi

LLL is a highly incapacitating potential side effect of cancer treatment that can severely reduce quality of life. LLL can be detected non-invasively with optoelectronic volumetry.

This study's primary objective was to determine the validity of the Lymphedema Functioning, Disability and Health Questionnaire for LLL (Lymph-ICF-LL) as a scale of LLL symptoms in cancer patients six months after lymph node surgery. The secondary objective was to compare methods for evaluating limb volume across objective methods, circumference measurements, and clinical evaluations. A sample of 84 patients with gynecological cancer or cutaneous melanoma with or without LLL completed the clinical evaluation, quality of life questionnaire, and leg volumetry with metric-tape perimetry; 55 of these patients also underwent optoelectronic volumetry.

The Lymph-ICF-LL was confirmed to be a valid tool for assessing quality of life in patients with cancer-associated secondary lymphedema. Considerable measurement bias was observed between the perimetry and optoelectronic volumetry; their results should be compared with caution because they are not interchangeable.

Acess here.

Establishment of a platform for renal cell carcinoma (RCC) studies based on xenografts in immunodeficient animals

Adriano de Oliveira Beserra

The use of patient-derived xenografts (PDXs) has emerged as a promising approach for the study of cancer biology and for the development of new anticancer drugs. RCC is the most common form of kidney cancer, accounting for up to 90% of all renal neoplasms.

RCC has a propensity for metastasis. It is estimated that some 25% of patients with RCC are diagnosed with advanced disease (local invasion and/or metastasis), and metastatic disease is generally incurable. In addition, up to 30% of patients with localized disease who undergo complete resection of the kidneys will have a recurrence. Therefore, this study's objective was to establish and develop a PDX resource to identify new biomarkers with which to monitor RCC and guide therapy.

Samples were obtained from the resection tissues of 73 patients treated surgically at A.C.Camargo. Tumor fragments were implanted in NOD Scid Gamma immunodeficient mice, either ectopically via subcutaneous injection (27 cases) or orthotopically via renal capsule (46 cases). When the tumors showed signs of growth detected by palpation, the animals were anesthetized, and their blood was collected. The tumor was removed, and a second passage was made. The tumor fragments were cryopreserved and underwent histology, immunohistochemistry, and genomic sequencing analyses.

The results indicated that the orthotopic PDX model for RCC was standardized with success and that it is an adequate tool for studying tumor biology in vivo. It was effective in preserving the tumor characteristics of the primary human tumor. Comparative characterization of the human tumors and the PDX tumors confirmed similarity in morphology, immune-histochemical marker expression, and genetic alterations. High-grade tumors with advanced pathological and/or metastatic staging showed better viability and growth in PDX models than less aggressive tumors.

The vitrification technique preserved tumor vitality effectively as evidence by the observation that that reimplantation did not alter the growth pattern observed during the implantation of fresh tumor samples. However, we did not obtain success involving RCC. It was not possible to perform the methods of analysis for VEs derived from animal plasma with renal tumor PDX.

Acess here.

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CREDITS

About the content of this report

The Scientific Production Report presents the knowledge production of the A.C.Camargo Cancer Center during 2019. The information in this publication condenses certain aspects of the institutional Sustainability Report, available here.

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