With a high concentration of laboratories and hospital facilities gathering more than 600 researchers and oncologists, Lyon has been able to play a leading role in the combat against cancer in France. Therefore the cancer patients in Lyon treated at Léon-Bérard Centre, the hospitals of the Croix Rousse and Edouard Herriot and at a large number of private clinics such as the Mermoz Clinic, already benefit from the impetus of this research. Here, we take stock of the advances made, cancer by cancer.

WHY LYON IS IN POLE POSITION IN THE FIGHT AGAINST CANCER

A dossier compiled by Véronique Lopes

Lyon mainly owes its national status in research and innovation in the fight against cancer to its glorious history. In 1923, Professor Léon Bérard, a Lyonnais, practicing at the Hôtel Dieu Hospital, developed cobalt bomb therapy, one of the first anti-cancer treatments in France. Later, in 1950, the Lyonnais doctor, Paul Santy, instigated the creation of a building capable of accommodating 300 patients next to the Edouard Herriot Hospital. This centre, which was to become the Léon Bérard Centre, was the first centre in the country to treat only cancer patients. Afterwards, driven in particular by the voluntarist policy implemented by Thierry Philip, the former director of the Léon Bérard Centre, the facility has developed to the point where it now counts about 500 researchers working in ten different units.

DYNAMIC RESEARCH However, chance was also to play a part. Following the Liberation, General De Gaulle decided to set up the International Agency for Research on Cancer (IARC) in Lyon in homage to a member of the Resistance whose wife was suffering from this disease. Thus small events in time can lead to changing history.

This entity, which now belongs to the World Health Organisation (WHO) and groups more than 300 researchers in Lyon, is the source of more than half of the publications on the subject in the world. Research is strongly represented in Lyon by different organisations (Ligue Contre le Cancer, the Institut National du Cancer, ARC), and by the local authorities.
They have provided nearly €42 million in funds to the cluster Cancéropôle Lyon Auvergne Rhône-Alpes (CLARA) since it was founded in 2003. There is nothing new in this support. The Rhône General Council was the first in France to finance breast cancer screening over 20 years ago. This generosity can be explained in part by the high number of doctors in the local authorities of Lyon, a characteristic that above all benefits the population of Lyon. Naturally, on paper the entire population of France is equal confronted by cancer, at least regarding the healthcare and treatment protocols specific to cancer plans. However, the concentration of research in Lyon represents an opportunity for the city’s population: new protocols can be offered to a patient followed up by a doctor participating in clinical tests. “There is a genuine link between research and the care provided to patients in Lyon,” says Thierry Philip, who emphasises the importance of “pooling experiences and communication between driving forces”.

A NEBULA The regional Cancéropôle cluster was set up ten years ago in view to facilitating exchanges between the actors combating cancer. Work remains to be done, though mentioning the many entities dedicated to research on cancer including the Léon Bérard Centre, the Hospices Civils de Lyon and the IARC (not forgetting the oncology and health cooperation group of the University of Lyon), Cancer Research Centre of Lyon, the Synergy Cancer Foundation of Lyon, the Integrated research site of Lyon, the Oncology and Haematology Therapy Investigation Centre of Lyon, etc.) brings to mind a rather nebulous and inconsistent mass.

“The organisation of research on cancer has to be optimised”, acknowledges Véronique Trillet-Lenoir, the President of the management board of the Cancéropole cluster. She considers that for Lyon, the challenge is henceforth to “unite its forces in order to remain present internationally”. The first exchanges between universities started several years ago, for example, between Lyon 1 and the Jiao-Tong University of Shanghai, which frequently join forces to work on liver cancer in China. The Japanese company Oncotherapy Sciences, specialised in the development of synovial sarcomas, set up its European subsidiary in Lyon in 2010. A sure sign of the sector’s vitality.
Modern techniques for curing cancers

Breast cancer

IMMEDIATE RECONSTRUCTION IS DEVELOPING

4,825 new cases a year in the Rhône Alpes region
53,041 new cases a year in France

HOW IS IT DETECTED? Breast cancer is the most common cancer in women. It is first revealed by mammography and echography and confirmed by carrying out a biopsy in the case of suspicious signs. Treatment includes surgery to remove the tumour or the whole breast, depending on the size of the tumour, as well as the sentinel lymph nodes (located under the arm). If necessary, the patient receives additional therapy in the form of chemotherapy and/or radiotherapy.

IT’S NEW Today, breast surgery is moving towards oncoplastic surgery which attempts to conserve the breast. Likewise, immediate breast reconstruction, which is to say the removal of the breast and its reconstruction during the same operation, is becoming standard practice. This technique provides better aesthetic results and the possible conservation of the cutaneous envelope. In 2012, 102 patients benefitted from immediate breast reconstruction out of 768 women followed up for non-metastatic cancer at the Léon Bérard Centre. However, certain breast cancers require delaying reconstruction by from six months to a year after the end of radiotherapy. Likewise, in the framework of a research protocol, some patients now benefit from radiotherapy performed directly in the opened breast during the operation, using the Intrabeam technology. This new technique used at the Léon Bérard Centre since 2012 permits treating a patient only once rather than prescribing radiotherapy sessions (25 on average) after the operation.

AND TOMORROW? At present, research on chemotherapy is in progress in view to finding treatments that target only cancerous cells. Analysis of the cancer’s genetic code may make it possible to customise patient treatment. In cases where all the sentinel nodes are removed by axillary node dissection under the armpit, one of the secondary effects can be the appearance of a lymphedema (swelling of the arm). Adapted intensive kinaesthetic techniques have now been developed to avoid this phenomenon. Nonetheless, tests are still being performed to avoid axillary node dissection and the resulting major discomfort it causes for the patient. Generally, research is taking the direction of less invasive treatments such as the destruction of cancerous cells without operation, notably by ultrasound and cryotherapy (using cold to destroy cancerous cells).

EFFORTS TO PROVIDE PSYCHOLOGICAL ASSISTANCE

Treating patients increasingly includes psychological treatment. Depending on the hospital, nurses specialised in diagnosis announcement, psychologists and “socio-aestheticians” are at the patient’s disposition without additional cost to provide them with as much information as possible before and after the operation and thus reduce their stress. Furthermore, an adapted physical activity programme, also free of charge, has been organised in the “Cancer and environment” unit of the Léon Bérard Centre. Since physical and sports activity have been recognised as being efficient for recovery and the reduction of relapses, patients are able to practice gym or Nordic walking twice a week for three months. The success of this programme, initially intended for women with breast cancer, has led to its being made available to other cancer patients.

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www.synergielyoncancer.com
Blood cancer

A EUROPEAN TEAM SOON READY FOR RESEARCH

2,082 new cases in the Rhône Alpes region every year
14,000 new cases in France every year

HOW CAN IT BE DETECTED? Blood cancers represent about 10% of all cancers and include lymphomas (cancers of the lymph nodes), leukaemia and myelomas. Lymphomas are the most frequent and about 14,000 new cases occur in France every year; however, the public knows little about this disease. Lymphomas are diagnosed in the laboratory by performing biopsies of tumours in order to determine the best treatment to be administered. Treatment mostly takes the form of chemotherapy which can be combined with immunotherapy.

IT’S NEW New treatments are now emerging thanks to the progress made in classifying the different forms of lymphoma and to the clinical studies performed by the team composed of Professors Coiffier and Salles at the South Lyon University Hospital. Certain clinical tests performed in Lyon are the first of their type in the world. There are two types leukaemia: chronic and acute. Patients with the former are mainly treated as outpatients while those with the latter undergo intensive chemotherapy and sometimes grafts of bone marrow or umbilical cord blood cells. It is noteworthy that the team of Professor Michalet of the South Lyon University Hospital was one of the first to propose grafting umbilical cord blood cells ten years ago.

AND TOMORROW? Lyon will soon have a new building to accommodate the European Lymphoma Institute (ELI) in the South Lyon University Hospital, where teams from seven countries will work. The aim is to organise clinical tests and train world class physicians. The first stone will be laid in 2014.
Renal cancer

THE ENHANCED DA VINCI ROBOT
PRECISION FIRST
875 new cases in the Rhône Alpes region every year
12,000 new cases in France every year

HOW CAN IT BE DETECTED? Since renal cancers are painless in the great majority of cases, they are often discovered by chance during radiological (echography or scanner) examinations. The risk factors of this cancer, which affects twice as many men as women, are arterial hypertension, tobacco and obesity. Treatments differ according to whether the cancer is metastatic or not. When at a localised stage (without metastases), it can be treated by surgery, by ablation of the tumour, by preserving the organ without the need to apply additional therapy such as chemotherapy, or radiotherapy.

IT’S NEW In most cases kidney surgery is done by laparoscopy a technique by which the instruments are passed through small incisions made in the abdomen. At the South Lyon University Hospital, patients can be operated by robotic laparoscopy using the Da Vinci robot (see photo). The surgeon sits behind a control console that provides 3D visualisation of the organs, leading to great precision in performing the operation. Otherwise, the team formed by Professors Paparel and Golfier at the same hospital remove the kidney via the vagina. This technique avoids making incisions and extracting the kidney via the abdomen. Thus post-operative pain is considerably reduced. For more fragile patients and patients with small renal cancers measuring less than 4 cm, alternatives to surgery can be proposed such as cryotherapy (treatment by cold at -40°C) and radiofrequency (treatment by heat at +100°C). However, the best results are obtained by surgery which remains the reference treatment, especially for young patients.

AND TOMORROW? An alternative method, stereotactic radiation therapy, is currently being evaluated. This innovative technique is used to deliver high doses of radiation while preserving the surrounding tissue as much as possible.

ENT Cancers
TRACHEOTOMY CAN BE AVOIDED
1,470 new cases in the Rhône Alpes region every year
17,000 new cases in France every year

HOW CAN THEY BE DETECTED? ENT cancers concern the mouth, the pharynx, the salivary glands and the sinuses. France is one of the countries most affected by this cancer for which the main risk factors are tobacco, alcohol and human papillovirus (the same virus as that of cervical cancer), due to the evolution of sexual practices (increased practice of oral sex). This cancer can have several symptoms: a change of voice, impeded swallowing, swollen lymph nodes in the neck, persistent ulcers. If a person suffers from such symptoms for more than three weeks, they should consult a
doctor. The chances of being cured are from 80 to 90% if the cancer is diagnosed early, and from 30 to 40% for advanced stages. The diagnostic is confirmed by a biopsy performed under local or general anaesthetic depending on the position of the tumour. Evaluating these tumours requires endoscopy under general anaesthetic, a scanner and sometimes IRM. In the case of small tumours, surgery or radiotherapy can be considered depending on the cause and position of the cancer. Surgery, radiotherapy and chemotherapy may be combined for the largest cancers.
IT’S NEW Since 2009, the team of professor Céruse of the South Lyon University Hospital has been performing pioneering work with minimal-invasive transoral surgery assisted by a robot. The latter is used to operate on organs that cannot be reached using classical surgical instruments, such as tumours at the base of the tongue, the larynx and the hypopharynx. This technique avoids performing a tracheotomy in nearly 80% of cases, thereby shortening the patient’s stay in hospital. They can also speak immediately afterwards and eat sooner than was possible before. For ENT cancers at a more advanced stage complex reconstruction surgery can be performed on a jaw or the tongue. In the future, it will be possible to consider transplants, such as that of the larynx.

AND TOMORROW? Regarding chemotherapy, treatments are evolving towards targeted therapies and treatments through the mouth (rather than intravenously) which are less costly and more comfortable for the patient. The use of nanoparticles could be generalised in just over ten years’ time.

The Lyonnais company Edap-TMS has developed Focal One which uses ultrasound focused at high intensity to destroy cancerous tissue in the prostate gland.

Prostate cancer

ABLATION OF THE TUMOUR RATHER THAN THE ORGAN

4,933 new cases in the Rhône Alpes region every year
70,000 new cases in France every year

HOW CAN IT BE DETECTED? Prostate cancer is the most common cancer in men. Today, although it affects more than 70,000 men a year, it is becoming increasingly synonymous with death. Fatality has decreased by 2.8% a year for the last ten years. Despite the fact that there is no way of preventing this cancer, over 80% of prostate cancers are detected at an early stage, in particular through screening blood samples for the prostate specific antigen (PSA) which permits identifying men at risk between 45 and 70 years old, and thus provide them with better care. Precise diagnosis of prostate cancer is performed by MRI examination of the prostate linked to biopsies oriented by the MRI data obtained. These examinations are used to classify the cancers into three groups of risk (low, medium and high). Cancers classified as “low risk” can be simply monitored to delay or avoid treatment by surgery or radiotherapy, which lead to the risk of urinary incontinence and/or impotence. Cancers classified as “medium risk” are treated by radical surgery (ablation of the prostate) usually performed by laparoscopy (possibly using the Da Vinci robot), by external radiotherapy or by installing radioactive implants. Since the prostate is a mobile organ particle accelerators are now equipped with a guidance system designed to target the areas to be treated with greater accuracy. Lastly, cancers classified “high risk” require treatments combining ablation of the prostate, radiotherapy or radiotherapy associated with hormonotherapy for a period of three years.

In cases of metastased prostate cancers, doctors can opt for hormonotherapy since the prostate is hormone sensitive. Hormone treatments imply chemical castration with secondary effects such as hot flushes and, in the long term, bone fragility.

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www.synergieyoncancer.com
IT’S NEW A new strategy called focal therapy is now being proposed to patients with small, low risk and intermediate risk cancers. Ablation of the organ can then be proposed or not. The cancer can be destroyed by different methods including cryotherapy (freezing the tumour) and high intensity focused ultrasound (destruction by heat). The Lyonnais company Edap-TMS has developed a device that uses high intensity focused ultrasound that destroys the cancer within the prostate gland.

AND TOMORROW? Today in Lyon, INSERM unit 1033 is working on the formulation of drugs to reduce the risk of bone fracture in metastatic prostate cancers.
Cervical cancer

THE CHANCES OF CONCEIVING CAN BE PRESERVED

244 new cases in the Rhône Alpes region every year
3,028 new cases in France every year

In 70% of cases, cervical cancer is caused by a virus called papillomavirus that mostly affects women between 45 and 55 years old, and for which a vaccine exists. At present in France it is estimated that at least 30% of young women are vaccinated against this cancer (versus 70% in Australia) which causes a thousand deaths a year.

HOW CAN IT BE DETECTED? Contrary to other cancers like breast cancer, cervical cancer is not screened in every region of France. It is therefore up to women to demand screening at least every three years after the age of 25, by a gynaecologist who performs a smear test to detect precancerous lesions. If dysplasias (precancerous lesions) are observed, the surgeon performs conization (ablation of part of the cervix) via the vagina. If the beginnings of a cancer are observed, the patient must undergo a full hysterectomy (ablation of the uterus, cervix and ovaries), if possible by laparoscopy as well as the ablation of a sentinel node possibly combined with radiotherapy or chemotherapy. For young patients expressing the desire to become pregnant, a procedure called tracheloctomy, popularised at the beginning of the 2000s in Lyon by Professor Dargent, allows the patient to conserve the uterus and thus the chances of conception.

Ovarian cancer

IMMUNOFLUORESCENCE SOON TO BE USED IN CLINICAL TESTS

386 new cases in the Rhône Alpes region every year
4,620 new cases in France every year

Ovarian cancer mainly affects women from 60 to 70 years old. As it gives rise to few symptoms, there is still no means of screening it, which is why about 70% of ovarian cancers are not diagnosed before reaching an “advanced” stage.
Preparation of biological samples in the laboratory of the Léon Bérard Centre.

In the case of diagnosis of suspected cancer, the doctor performs an examination by imaging (echography, thoracic-abdominal-pelvic scanning, MRI of the pelvis), then a biopsy by laparoscopy. The therapeutic strategy relies on surgery by laparotomy, that is to say an incision in the abdomen combined with chemotherapy.

AND TOMORROW? Research resulting in better understanding of cancer mechanisms has led to the development of new molecules and many clinical tests are in progress in view to proposing more individualised treatments. Regarding surgical research, the use of Intra Peritoneal Chemo Hyperthermia (ICPH), used in particular in digestive cancers, is now being assessed for relapses of ovarian cancer. Furthermore, following works in experimental surgery, the use of immunofluorescence, meaning the use of an injected product that turns fluorescent when in contact with a cancer, should reach the clinical test stage soon. Lastly, the Léon Bérard Centre has one of the only reference centres of rare ovarian cancers. This service allows doctors from all over France to present rare cases and thus benefit from specific expertise.

Endometrial cancer
TOWARDS MINI-INVASIVE SURGICAL TECHNIQUES
646 new cases in the Rhône Alpes region every year
7,275 new cases in France every year

Endometrial cancer mainly affects menopausal women. The symptom is vaginal bleeding. No screening exists as yet though the symptomatic nature of this cancer leads to care being given at an early stage in 80% of cases. The first treatment is surgical. It consists in the ablation of the uterus, the cervix and ovaries, associated with the more or less total removal of adjacent lymph nodes. These surgical operations are done increasingly by laparoscopy, a widespread surgical technique in the Lyon region. If the patient requires other treatment following surgery, they can be given external radiotherapy or chemotherapy by natural intake, with limited secondary effects. Less aggressive techniques for searching for sentinel lymph nodes are now being developed and show promise for very early stages of the disease.

Colon and rectal cancer
SCREENING TO OPTIMISE THE CHANCES OF TREATMENT
3,890 new cases in the Rhône Alpes region every year
40,000 new cases in France every year

Diagnosing this cancer is difficult, since the patient displays few symptoms. It can be detected by endoscopy, or by colonoscopy combined with a biopsy coupled with abdominal echography. It is generally characterised by the presence of blood in the faeces, intestinal transit problems or abdominal pains. If detected at an early stage, colon-rectal cancer can be treated by the ablation of polyps by endoscopy. In advanced cases, surgery may be combined with radiotherapy for the rectum and with chemotherapy for the colon. Regarding prevention, screening is organised but difficult to implement. In the Rhone department, the association Ademas 69 is responsible for sending several letters to persons between 50 and 74 years old, proposing that they take a test that consists in sending a sample of their faeces for analysis. To date, only 30% of the population has responded to this test, making it difficult to provide care at advanced stages.
Peritoneal cancer

ICPH IN SUPPORT OF SURGERY

Regarding cancers of the peritoneum, meaning the fine membrane that covers the abdominal cavity and the organs contained in the abdomen, the team of Professor Gilly of the South Lyon University Hospital has developed a technique that combines surgery and chemotherapy. Performed at the same time as surgery, this treatment called Intra Peritoneal Chemo Hyperthermia (ICPH), consists in “bathing” all the surfaces of the organs in the abdominal cavity with a chemotherapy product heated to 42°C. The heat and chemotherapy destroy the microscopic cancer cells. This operation is performed “stomach closed” via drains.

* The general, digestive, endocrine system surgery department of the South Lyon University Hospital is the national reference centre for rare peritoneal cancers.

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“Investors hesitate to finance innovation”

INTERVIEW Sylvie Negrier, General Manager of the Léon Bérard Centre, is also a professor at the University of Lyon and a medical oncologist

Does Lyon play a leading role in cancer research in France?
Sylvie Negrier: Yes. After Paris, Lyon is the most active and visible city regarding research and innovation. It’s also the French city with one of the largest research centres specialised in cancer biology.

However, considered internationally, Lyon does not appear to be that visible.
That’s true. Even though Lyon has started to win recognition for its works at international level, notably thanks to certain researchers such as Professor Coiffier, who heads the European Lymphoma Institute based at the South Lyon University Hospital, or Professor Blay, who coordinates the World Sarcoma Network from Lyon. But we’re only just starting. Becoming a major actor at international level is the result of a long term policy. We’ve passed the first stage of reaching a critical mass of researchers. The next stage is to attract the competences we don’t have to make the transition from research to clinical application.

What are the factors that slow down this growth?
At present, we’re coming up against real difficulties in financing translational research. That’s to say research that transcribes the discoveries made by researchers into treatments for patients. This type of research is not financed by the Ministry of Research but through the donations and legacies that we receive and through support from local authorities. In France we also lack biotech companies, contrary to the United States. For all that, we need these companies to develop the products, drugs and equipment that we can then validate with the patients. Many companies start up in the region and fail to last more than 5 to 7 years. It’s often because bankers and investors hesitate to finance innovation. Unfortunately, this phenomenon has worsened in the current economic climate.

“Becoming a major actor at international level is the result of a long term policy”, explains Sylvie Negrier.