



Netherlands Cancer Institute - Antoni van Leeuwenhoek Hospital

Edition - 2006

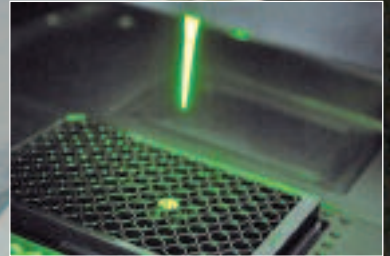


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Introduction

The Netherlands Cancer Institute – Antoni van Leeuwenhoek Hospital (NKI-AVL), of which Queen Beatrix of the Netherlands is patron, combines a scientific research laboratory with a specialised clinic. Since its foundation in 1913, the primary objective of the NKI-AVL has been to make a substantial contribution to combating cancer through a unique interaction of scientific research and clinical application, supported by strong training. More specifically, it has the following goals:

- To ensure high quality diagnosis, treatment and nursing care for the prevention and treatment of cancer. To develop new methods and continuously improve existing ones, so that cancer can be diagnosed and treated at the earliest opportunity, and the patient's burden reduced.
- To conduct a broad spectrum of cancer-related research comprising fundamental biological studies as well as clinical, epidemiological and psychosocial research. The institute's ambition is to be a leader in the international scientific field.
- To expand skills in the prevention and treatment of cancer, both within the institute and externally, by transfer of knowledge and education and training of physicians, scientists and other professionals in the field of oncology.
- The NKI-AVL collaborates with academic (teaching) hospitals, universities and scientific research institutes both in the Netherlands and abroad. It plays an important role, both nationally and internationally, in oncology research, oncological treatment and care and in the training of highly qualified scientists, medical specialists, nurses and auxiliary care providers in the field of clinical oncology. The NKI-AVL is internationally recognised as a Centre of Excellence in the field of cancer.



The clinic

The medical team of the NKI-AVL works tirelessly to improve the prognosis and quality of life of cancer patients (see Box Cancer). Central to this aim is the search for earlier and more efficient diagnosis. The close cooperation between the research institute and the clinic in applying clinical research is enhanced by the fact that medical specialists, nurses, scientists and patients all work under one roof. Investigations can therefore be initiated quickly, results obtained and treatment implemented in the clinic without delay.

Top oncology centre

The NKI-AVL diagnoses and treats cancer patients from all over the Netherlands. 25 per cent of the care provided consists of highly sophisticated cancer treatment, while 60 per cent of patients are referred to the institute by specialists in other parts of the country and 15 per cent relates to care for patients from the Amsterdam region.

Extensive diagnostic facilities

NKI-AVL specialists have access to a wide range of facilities for the diagnosis of cancer. The departments of pathology, radiology and nuclear medicine and the clinical laboratory use many different diagnostic tools. The Familial Tumour Clinic investigates the risk of hereditary forms of cancer with the aid of questionnaires, interviews and if necessary, DNA diagnosis. The Congenital Tumour Clinic has many years of experience in tracing families in which congenital forms of cancer occur, and in advising members of those families on their treatment options.

Multidisciplinary approach

The NKI-AVL takes a multidisciplinary approach to the diagnosis and treatment of cancer. A team combining all areas of clinical expertise – for example, surgeons, radiotherapists and pathologists, as well as oncology nurses and paramedics – discusses each tumour type and decides on the best treatment. Various specialists then monitor the patient's progress, to ensure that he or she continues to receive the best treatment.



Tailored treatment

The treatments at the NKI-AVL often consist of a combination of surgery, chemotherapy, hormone therapy and/or radiotherapy, plus various specialised treatments. This combined approach improves local control of tumours and eradication of distant metastases while, as far as possible, conserving organs. Although most of the treatments are designed to cure cancer, palliative treatments (treatments aimed at alleviating the symptoms of the cancer) are also used. Examples of palliative treatment include operations to reduce the mass of an incurable tumour and so relieve pain or occlusion, pain-reducing radiotherapy and the insertion of an endoprosthesis or tube into the oesophagus or bile duct to enable the patient to eat and drink.



Cancer

Cancer is a disease that occurs when cells divide and grow in an uncontrolled fashion. This results in a swelling or tumour that can prevent the normal function of vital organs. The abnormal cells may also spread through the body by a process called metastasis, via the blood or lymph system, and damage other essential systems. Because cancer arises out of normal cells, it can develop in almost any organ or tissue.

Specialised treatments

Many different specialised treatments are provided at the NKI-AVL. These include:

- **Robotic assisted surgery** Since recently it is possible in the NKI-AVL to operate with the Da Vinci S. Robot, on patients with localized prostate cancer. It is not the equipment that works by itself, but it is always controlled by a surgeon. It has four robotic arms. The robot technique is a refinement of the laparoscopic operation techniques. The complete operation is carried out by making five small incisions in the abdomen. Because of the flexibility and movability of the robotic arms it is possible to perform very specific tasks in a small area. Due to stereoscopic imaging the surgeon has a three dimensional and magnified view of the surgical field. Scientific studies suggest several major advantages of using robotic assisted surgery: less loss of blood during operation, decreased treatment duration, outstanding results with regards to preservation of erectile function and sphincter function of the bladder. With the robotic assisted surgery, the NKI-AVL has all surgical and radio therapeutic treatments under one roof.





- **Bladder reconstruction** In the past, a patient whose bladder had to be removed due to bladder cancer was given a stoma, or artificial opening in the abdominal wall, to allow him or her to pass urine. Since 1989, however, it has been possible to fit such a patient with a bladder-like reservoir for the natural collection and passing of urine. Since 1995, this technology has become so refined that the reservoirs now reproduce the function of the bladder almost perfectly. They are implanted surgically, and work so well that most patients can even enjoy a normal sex life.
- **Brachytherapie** In this form of therapy, the tumour is irradiated not from an external source as in conventional radiotherapy, but from a radioactive source introduced into the body via a catheter or needle. In this way the source can be positioned in, or in close contact with, the tumour, so that it delivers a high and accurately pinpointed radiation dose. Brachytherapy is often used when the tumour in question requires a high dose of radiation and is situated near organs that could be damaged by that radiation. It may also be employed to eradicate tumour residues left behind after surgery.
- **Photodynamic therapy (PDT)** This light-based therapy involves administration of the photosensitive substance Foscan. When the tumour is irradiated with laser light, the Foscan is activated and causes the blood vessels feeding the tumour to close up. Deprived of a blood supply, the cancer cells die. Unlike surgery or radiotherapy, PDT has no adverse side effects such as the formation of scar tissue. PDT is mainly used for head and neck tumours, and studies have shown that it eliminates 87 per cent of small tumours in this region. So far, the NKI-AVL is the only centre in the Netherlands to use PDT on a regular basis.

- **Hyperthermic intraperitoneal chemo therapy (HIPEC)** The HIPEC operation is used in the treatment of cancer of the large intestine with metastases in the peritoneal cavity and peritoneum (the membrane that lines the abdominal and pelvic cavities), and of myxomas originating in the appendix or ovaries. The operation consists of the surgical removal of the tumour and associated tissue from the abdomen, followed by flushing of the peritoneal cavity with a highly concentrated, warm mixture known to kill the cancer cells remaining on the peritoneum.
- **Image guided radiotherapy** One of the latest types of irradiation equipment, the cone beam computerised tomography (CT) linear electron accelerator, was installed in the radiotherapy department of the NKI-AVL in 2003. With this equipment, the clinician can view a three-dimensional (3-D) scan of the patient during irradiation, making it possible to target tumours that move (for example, as a result of respiration) with higher precision and higher radiation doses. The tumour boundary is always visible during treatment.
- **Intensity modulated radiotherapy** Using the advanced irradiation equipment available in the radiotherapy department, this therapy can be tailored to the 3-D shape of the tumour by modulating the intensity of the



radiation. This means that a higher radiation dose can be delivered to the tumour while the radiation exposure to surrounding normal tissues is minimised. Tumours in the head and neck, for example, are irradiated with up to 40 narrow beams to avoid organs including the salivary glands, thereby reducing the risk of unpleasant side effects such as a dry mouth.





- **Combined chemotherapy and radiotherapy**

An example of combined chemotherapy and radiotherapy is the RADPLAT treatment. Until a few years ago, patients with large tumours in the head and neck region received extensive surgery followed by seven weeks of radiotherapy. The treatment nearly always left visible scars and often had a severely adverse effect on the patient's quality of life. An alternative form of treatment, developed in the United States, was introduced at the NKI-AVL in 1997. RADPLAT combines seven weeks of radiotherapy (RAD) with direct infusion of the chemotherapy drug cisplatin (PLAT) to the site of the tumour. RADPLAT appears to improve the patient's chances of survival, without leading to the deterioration in quality of life that was seen with the traditional procedure.

- **Regional isolation perfusion** This therapy is used for patients with melanoma or skin cancer and metastases (secondary growths) in the arms or legs. First, the circulation of the affected limb is isolated from that of the rest of the body. The limb is connected to a heart-lung machine to provide it with its own supply of oxygenated blood, and is then perfused with chemotherapy drugs. A very high dose of these drugs can be used since vital organs in the rest of the body will not be affected. In this way it is possible to remove metastases completely in about 70 per cent of melanoma patients.

- **Sentinel node procedure** In certain forms of cancer, such as breast and skin cancer, the first metastases develop in one lymph node close to the tumour – the 'sentinel node' – before spreading to distant sites. If this node contains tumour cells, it may be necessary to remove the other lymph nodes – a far-reaching procedure that can have serious adverse effects for the patient. If it doesn't, this procedure can be avoided. The NKI-AVL pioneered the development and improvement of the sentinel node procedure for detecting whether this node contains metastasised tumour cells. For a long time, this procedure could only be used with breast tumours that were large and palpable, but in 1999 the Radioguided Occult Lesion Localisation (ROLL) procedure was introduced, which meant that it could also be applied to small, non-palpable breast tumours.





Patient care

Patients at the NKI-AVL are looked after before, during and after treatment by nurses who are specialised in the care of cancer patients. These oncology nurses play a pivotal role in the care of the patients assigned to them, from admission to discharge. Because the treatment patients receive can often be challenging, both physically and mentally, the NKI-AVL also employs a range of auxiliary care providers including dieticians, physiotherapists, stoma nurses, speech therapists and dental hygienists.

The patient support unit – comprising psychologists, social and pastoral workers, a psychiatrist, information officers, transfer nurses and creative therapists – offers patients and their relatives advice and psychosocial support in dealing with cancer. Volunteer groups, including the independent NKI-AVL Patient Care Foundation, also provide a range of support services to patients. The guest house next to the institute provides accommodation for relatives and out-patients who would otherwise have to make several long return trips each week.

New accommodation

In September 2003, the NKI-AVL expanded into a new hospital building situated next to the existing premises. This 180-bed building has all the latest facilities. Patients are accommodated in single or double bedrooms, each with its own TV and Internet link. They eat in their own buffet restaurant, and have their own roof garden on the seventh floor. They can also use the patients garden.

On the second floor, where the operating theatres and the intensive care unit are located, one operating theatre has been designed to allow patients to be irradiated during operations, while the tumour is exposed.





The new outpatient clinic on the ground floor has a unique layout reflecting the multidisciplinary approach to cancer treatment taken at the NKI-AVL. The consulting rooms, also on the ground floor, are linked to clinical staff offices on the first

floor by four staircases, thus facilitating interaction. Now that the new hospital building is operational, the old building will be renovated and will house the research departments. The entire renovation programme is expected to be completed in 2010.



Research

It is impossible to influence the behaviour of cancer cells without a deep understanding of how both cancer and normal cells work. Hence, much of the research carried out at the NKI-AVL is of a fundamental nature, in fields such as genetics and molecular and cellular biology. The institute also conducts clinical, translational, epidemiological and psychosocial research.

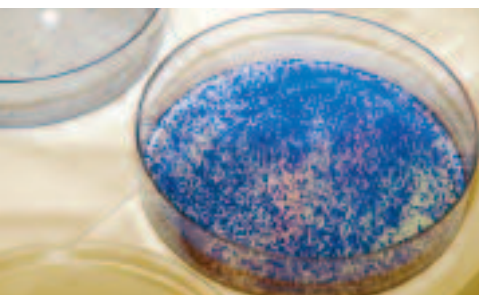
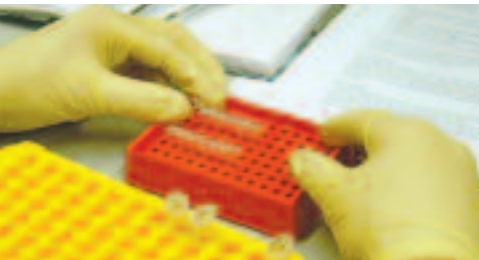
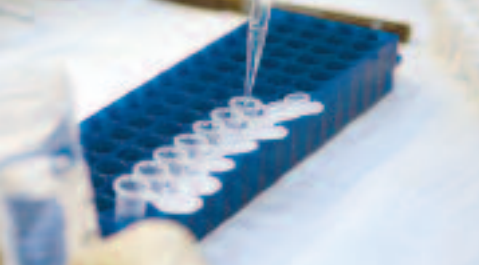
NKI-AVL scientists collaborate closely with teaching hospitals, universities and scientific research institutes in the Netherlands and Dutch research organisations: the Centre for Biomedical Genetics (together with the University of Utrecht, the Hubrecht Laboratory, Erasmus University in Rotterdam and the University of Leiden), and the Cancer Genomics Centre (together with the Utrecht Medical Centre, the Hubrecht Laboratory and the Erasmus/Daniël den Hoed Medical Centre in Rotterdam). The NKI-AVL has an extensive scientific library specialising in publications on cancer-related topics, designed to support the activities of the medical, paramedical and research staff.

Fundamental research

Normal cells turn into cancer cells as a result of changes in the cell's DNA, or genetic information, which lead to uncontrolled cell division and growth. The fundamental research at the NKI-AVL therefore aims to answer such questions as how defects arise in genes, which genes are involved in the development of different types of cancer, what is the normal function of those genes and whether drugs can be found that will selectively destroy the cells carrying genetic defects. This fundamental research falls into several categories:

Cell division

The genes that regulate cell division are defective in nearly all cancer cells, which is why these cells grow and multiply so rapidly. These genes are responsible for specific cell properties such as the cell's dependence on growth factors. Scientists identify these genes with the aid of special techniques, including functional screens (see Box Functional screen) – an area in which the institute has built up a great deal of expertise. A better understanding of the way cells divide could lead to new therapies based on slowing down abnormally fast cell division.



Functional screen

With the sequencing of the human genome, it is now possible to alter individual genes and so identify their function. The NKI-AVL uses several techniques for altering gene function, such as RNA interference (see Box RNA interference). When these are applied to model systems derived from human or mouse cells, scientists can study how the genetic modification affects cellular characteristics such as division and growth. In this way they can characterise the genes that play important roles in cancer, as well those genes that influence cells' sensitivity or resistance to therapy. This information in turn helps them to develop new and better anti-cancer drugs.

Communication between cells

When the communication within and between cells is disturbed, cells can no longer properly process signals in their immediate environment – signals telling them to slow down their growth, for example. A growth-retarding signal may not reach a cancer cell, or it may reach the cell but then be translated into an inappropriate behaviour. Defects in this sort of communication can lead to uncontrolled cell division and metastases.

Cell regulation

Cancer cells derive their malignant properties from control proteins, which may be present in the cells in excessively small or large quantities as a result of disturbances in their rate of synthesis or breakdown. The protein breakdown process is closely related to the immune system, which detects cells undergoing changes that result from protein breakdown and eliminates them. Studying this process helps scientists understand how cancer comes about and also yields insights into the background of other serious conditions such as Alzheimer's disease.

RNA interference (RNAi)

RNAi is an ancient cellular immune system that uses small pieces of RNA – genetic material related to DNA – to target and silence protein-coding genes of intruders such as viruses. Scientists have now harnessed this mechanism to selectively switch genes off and determine the effects of that gene silencing on cell function. This in turn allows them to identify the normal function of the gene. The NKI-AVL has a collection of 30,000 small RNA pieces, each of which switches off one gene. The collection, called the RNAi library, allows scientists to rapidly identify genes involved in the repair of damaged DNA, or to identify potential protein targets for drug development.

Drug resistance

A common problem in cancer treatment is the resistance or insensitivity some patients show to certain drugs. Research into the way this resistance arises is being carried out with the aim of finding ways to prevent and/or circumvent it. One phenomenon of interest involves the mechanism by which proteins 'pump' drugs out of cancer cells. NKI-AVL scientists have discovered that protein pumps in the intestine interfere with the normal uptake of chemotherapy. As a result of this, drugs have now been designed that transiently inhibit these pumps, allowing patients to receive their chemotherapy orally rather than by infusion, and so reducing their treatment burden (See *Translational Research*).

Stability of DNA

DNA is often exposed to damaging agents, including environmental toxins. Since DNA encodes instructions for how the cell should behave, damage to it can lead to disturbances in cell function, including cancer. Research into the causes and consequences of DNA errors is important both for the prevention and for the treatment of cancer. If defects can be identified, methods can be devised for effectively destroying the cells that contain them.

Immune system

The immune system can detect very slight differences between cancer cells and normal cells. Immunological research may lead to the development of new ways of stimulating the immune system to seek and destroy cancer cells (See *Translational Research*).

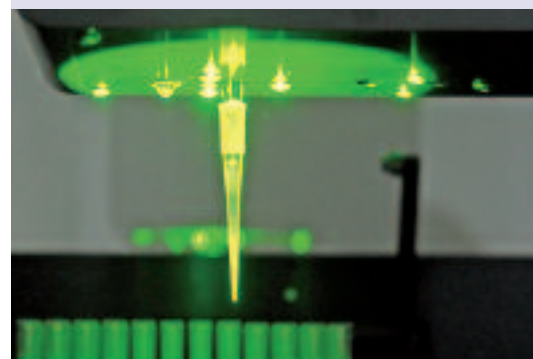
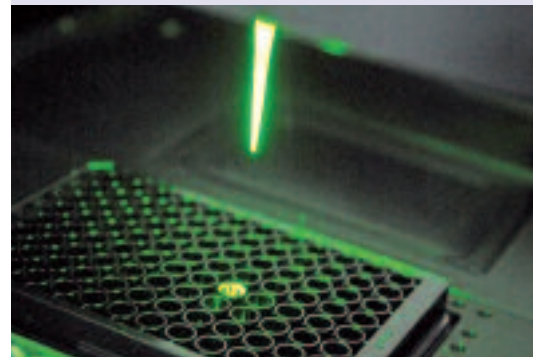
Development of animal models

A primary objective of fundamental research in oncology is to develop good model systems in which cancer can be studied. Targeted genetic modifications in mice, using RNAi for example,

have provided a means of accurately simulating an increasing number of cancers. As a result, mouse tumour models have become a much more precise tool for the study of cancer than was previously the case (see Box *Mimicking lung cancer in mice*).

Mimicking lung cancer in mice

Mortality from lung cancer is higher than for all other cancers. Part of the reason for this is that lung cancer tends to be diagnosed relatively late – after it has spread to distant sites and local treatment with surgery or radiotherapy have ceased to be effective. Chemotherapy is therefore required, but there is currently no effective chemotherapy against lung cancer. Even if the tumour initially gives a good response, it subsequently recurs. Recurrent disease responds less well to chemotherapy, since by then the tumour has become resistant. Good models of the development of lung cancer and of drug resistance are therefore very important. This is why mouse models for two common forms of lung cancer, small cell lung cancer (SCLC) and non-small cell lung cancer (NSCLC), have been developed at the NKI-AVL, by inducing the same genetic defects in the mouse that are found in human lung cancer. Using these mouse models scientists can study how various genetic defects contribute to the characteristics of the tumour, including resistance to treatment, and identify new targets for drug intervention. Mouse models can also be used to evaluate the efficacy of therapy at different stages of cancer. The growth and regression of tumours can be followed in a simple and non-invasive way, using a light-emitting enzyme obtained from fireflies. This improves the accuracy of the experiments, so that fewer animals are required.



Clinical research

Between 70 and 80 clinical trials, involving some 800 patients, are carried out at the NKI-AVL each year. Most of these are phase 1, 2 or 3 studies of potential new treatments or combinations of treatments (see Box Pharmaceutical clinical trials). Clinical trials are often performed in cooperation with other research institutes and hospitals in the Netherlands and abroad, and with the

pharmaceutical industry. The NKI-AVL also carries out phase 1 and 2 studies for the Brussels-based *European Organisation for Research and Treatment of Cancer*. The institute has its own data centre which supports clinical studies, for example by providing tools for data management and statistical analysis. Since 1953 the data centre has also kept detailed clinical records of all patients treated at the NKI-AVL.

An example of a therapy that is now in regular use at the NKI-AVL as a result of having successfully passed through clinical trials is combined radiotherapy and chemotherapy. The introduction of radio-chemotherapy has led to important advances in the treatment of many cancers over the past few decades, especially when the two are used simultaneously. Improvements have been shown for cancers of the head and neck, oesophagus, anus, lung and cervix, and more recently for stomach cancers. In addition to improving local tumour control and survival, radio-chemotherapy can sometimes lead to sparing of organ function. Although it is often associated with increased acute side effects, there are no increased long-term side effects. Radio-chemotherapy is an intensive and complicated treatment which involves different medical specialties. Treating the side effects also requires specialised medical and nursing experience. For these reasons, radio-chemotherapy patients are treated in a specialised department at the NKI-AVL.

Translational research

The NKI-AVL strives to ensure that information obtained through fundamental research is translated into clinical applications as quickly as possible. An example of successful translational research is the recent clinical trial on the use of aspirin ointment for the treatment of cancer of the hair follicles, which was set up immediately after scientists discovered a new function of an important cancer gene. Another example is the development of a class of drugs that is taken in combination with chemotherapy, to increase its uptake from the intestine. NKI-AVL researchers discovered that certain cellular transport mechanisms in the intestine prevent the uptake of anti-cancer drugs, which explains why traditionally, the oral route has proved a relatively ineffective means of delivery. Drugs have now been designed that transiently inhibit those

Pharmaceutical clinical trials

Pharmaceutical clinical trials are commonly classified into four phases. If the therapy or therapy combination successfully passes the first three phases, it will usually be successfully approved for use in the general population.

Phase 1: the first stage of testing in human subjects. In the case of cancer therapies, this tends to involve small groups (20 to 80) of patients with advanced or metastatic cancer. Trials assess the safety and tolerability of a therapy, among other things.

Phase 2: assesses the clinical efficacy of a drug in larger groups (100 to 300), as well as continuing Phase 1 assessments.

Phase 3: the definitive assessment of the efficacy of a new therapy. Involves large (1000 to 3000 or more subjects), randomised, double-blind controlled trials, in which neither patients nor investigators know which subjects have received the experimental therapy and which are acting as controls.

Phase 4: post-launch safety surveillance of a therapy.



mechanisms, removing the barrier to absorption. This means that patients can receive their chemotherapy orally rather than intravenously as in the past, and that in turn reduces their treatment burden. The advance is particularly important because changes in oncology mean that chemotherapy regimes have been intensified, with patients often receiving anti-cancer drugs once a week rather than once every three weeks as in the past. New anti-cancer drugs have also been developed that must be taken daily if they are to produce their anti-cancer activity. In both cases oral rather than intravenous administration is desirable or even necessary. The uptake-enhancing drugs are now being used successfully at the NKI-AVL in combination with the important anti-cancer drugs paclitaxel, docetaxel and topotecan.

Immunology has a long history at the NKI-AVL and within immunology, translational research is well-defined. The goal of this research is to develop effective immunological therapies in animal models and to translate them as rapidly as possible to the clinic. Immunotherapy

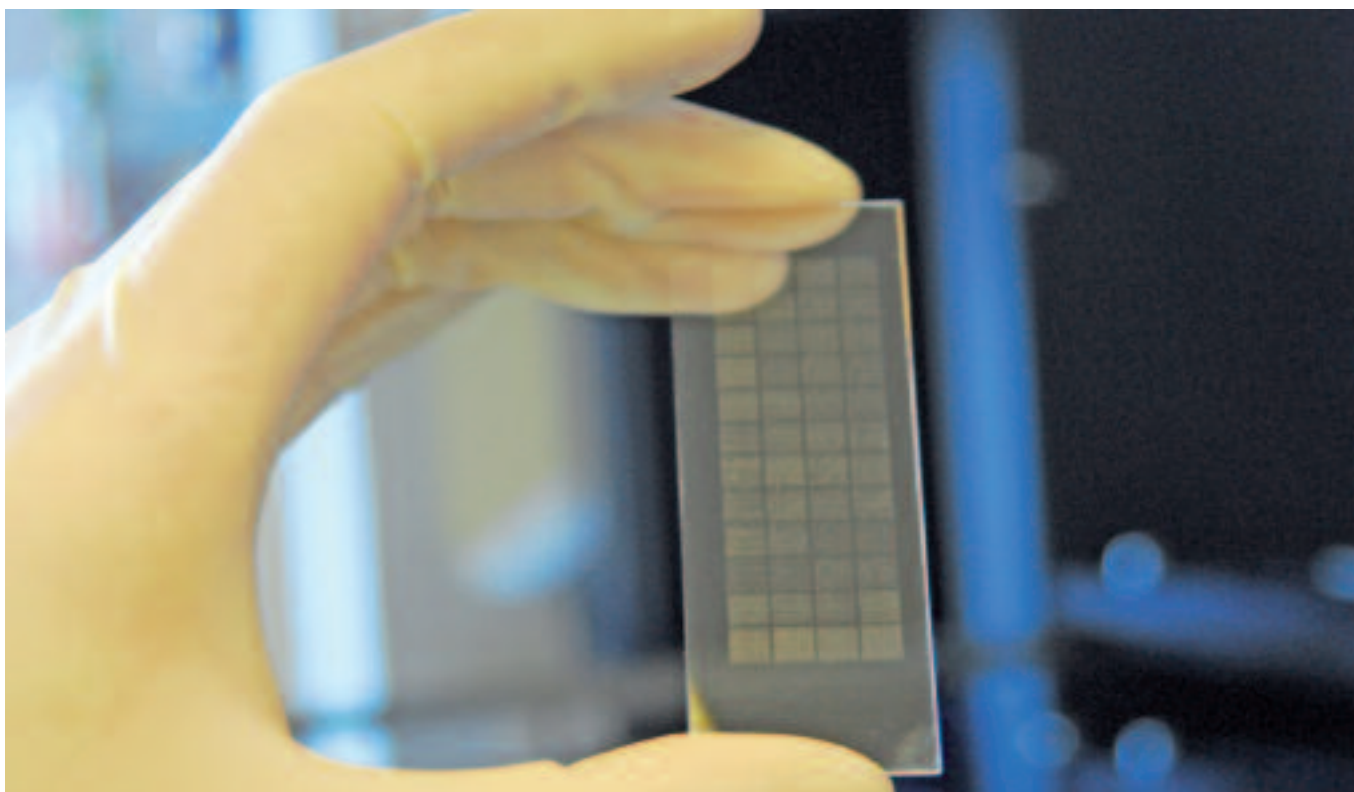
strengthens the body's immunity or natural defences to cancer, and it does so in two principal ways:

- Active immunisation, using anti-cancer vaccines. The patient is injected with tumour antigens, small molecules that cancer cells carry on their surface and that are recognised by the immune system. This should result in activation of the patient's immune cells against the tumour, and hopefully lead to tumour regression or provide long-term protection.
- Passive immunisation – by the injection of antibodies to tumour cell antigens, or by injecting anti-cancer immune cells. Since the patient's own immune response has failed, the goal of passive immunisation is to restore or strengthen that immune response to cancer.

It is possible that a combination of both approaches may prove to be most effective. Phase 1/2 clinical trials will soon be starting at the NKI-AVL for patients with advanced

stage melanoma. Both anti-cancer vaccines and injection of specific anti-melanoma immune cells will be tested.

An important problem in the treatment of cancer with radiotherapy and chemotherapy is that clinicians do not know in advance whether the cancer cells will be sensitive to these treatments. They do know, based on previous studies, if a specific tumour type is generally more or less sensitive to radiotherapy or chemotherapy, but a test to determine which treatment will most benefit an individual patient is not available. The NKI-AVL, in collaboration with an American research group, Rosetta Inpharmatics of Kirkland, Washington, has developed a test based on microarrays (see Box *Microarray test*) that helps clinicians decide whether additional chemotherapy is necessary after surgery for breast cancer. The Netherlands was the first country to initiate clinical trials of this test. In addition, the NKI-AVL has developed microarray tests that can potentially predict whether a breast cancer patient requires high dose radiotherapy after surgery, whether additional



anti-cancer drugs should be given to the patient and, if so, which drug and on which dosing schedule. This research project is being carried out in collaboration with a large number of Dutch hospitals. Similar predictive tests for other tumour types are at an earlier stage of development but look promising. These developments contribute to the increasing personalisation of anti-cancer treatment and should eventually lead to improvements in patient survival.

Microarray test

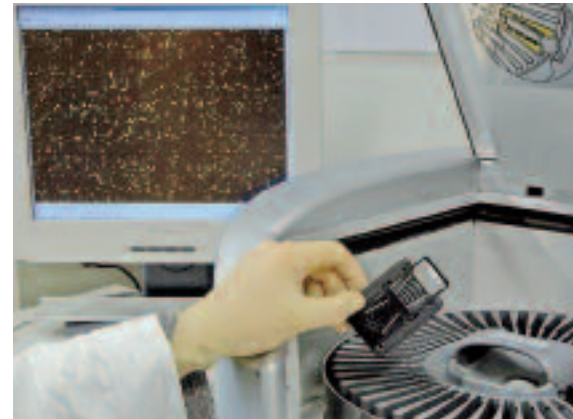
A tumour differs from healthy tissue in that certain genes are more or less active in it. This altered pattern of gene activity, which determines the tumour's behaviour, can be measured with microarrays. The microarray, or DNA chip, is usually a glass plate of 2 by 6 centimetres, on which 10,000 spots of synthetic DNA are arranged. Each DNA spot corresponds to one human gene. The first step is to extract RNA from the tumour. RNA (or more specifically, a type of RNA called messenger RNA) can only be extracted if the corresponding gene is active. Pieces of RNA from healthy tissue, or from a mixture of tumours, serve as reference material. The RNA is tagged with fluorescent dyes: red for the tumour and green for the reference material. The pieces of RNA bind to the DNA spots on the chip. RNA from an activated gene selectively binds to the corresponding DNA sequence. This can be visualised when the chip is illuminated with laser light. If the spot fluoresces green, the corresponding gene in the tumour is less active than in the reference material. If it fluoresces red, the gene in the tumour is more active. From the pattern of red and green spots, researchers can determine the pattern of gene activity of the tumour, and predict whether a patient will develop metastases. The treatment of breast cancer patients can be adjusted accordingly.

Epidemiological research

Epidemiological studies investigate the influence of lifestyle, environmental factors and medical treatment on the onset or recurrence of cancer. Such studies can play an important role in cancer prevention. Long-term epidemiological studies carried out at the NKI-AVL address such topics as risks associated with use of the synthetic hormone DES (diethylstilbestrol), the contraceptive pill and growth hormones, and the long-term effects of in vitro fertilisation (IVF) treatment.

Psychosocial research

The central question addressed by psychosocial researchers at the NKI-AVL is how the patient's well-being can be improved. Examples of investigations in this field include patients' attitudes to different methods of pain relief, their perception of different treatments and the extent to which they comply with them, and how patient-doctor relationships and communication can be improved.



Education and training

Education and training are a very high priority at the NKI-AVL, to ensure that staff remain fully qualified in a rapidly changing world. Many professionals also pass their knowledge and expertise on to healthcare workers and scientists outside the NKI-AVL. About 30 faculty members of the NKI-AVL are professors at Dutch universities, and members of the medical and research departments contribute to courses and symposia at universities and schools.



Doctoral and postdoctoral education

The Oncology Graduate School in Amsterdam, in which the NKI-AVL participates along with the Academic Medical Centre in Amsterdam (AMC) and the VU University Medical Centre in Amsterdam, provides doctoral and postdoctoral education. The NKI-AVL also cooperates with the AMC in running a two-year training course for medical students who have completed their basic training and wish to specialise in oncological surgery. They spend one year of the course working at the AMC and one year at the NKI-AVL. The NKI-AVL also provides a course in medical oncology, a sub-specialisation of internal medicine, and another in clinical pharmacology.

Professional development courses

The NKI-AVL offers training courses in professional development for a wide variety of people working in cancer care. These include a course for radiotherapy laboratory technicians; an advanced course in oncology nursing; specialist courses for radiotherapists, plastic surgeons and urologists; advanced courses for surgeons,





ear, nose and throat specialists and internists, as well as ongoing education and refresher courses for medical oncologists. The NKI-AVL also offers courses designed to help staff keep abreast of developments in the dynamic world of medicine, such as an on-the-job training course for nurse practitioners and courses

aimed at developing cooperative and communication skills. The latter include a management course and a course on learning how to deal with ethical dilemmas. Finally, the NKI-AVL offers work experience opportunities for students in relevant fields.



Organisation

The day-to-day management of the NKI-AVL is in the hands of the Board of Directors, which also bears final responsibility for the institute's general activities. Individual board members are assigned the 'scientific policy', 'care and care development' and 'organisation and management' portfolios. The Board of Directors is appointed by the Board of Governors, which supervises the policy and general running of the NKI-AVL.

Management of the primary activities of the NKI-AVL is divided between five organisational divisions:

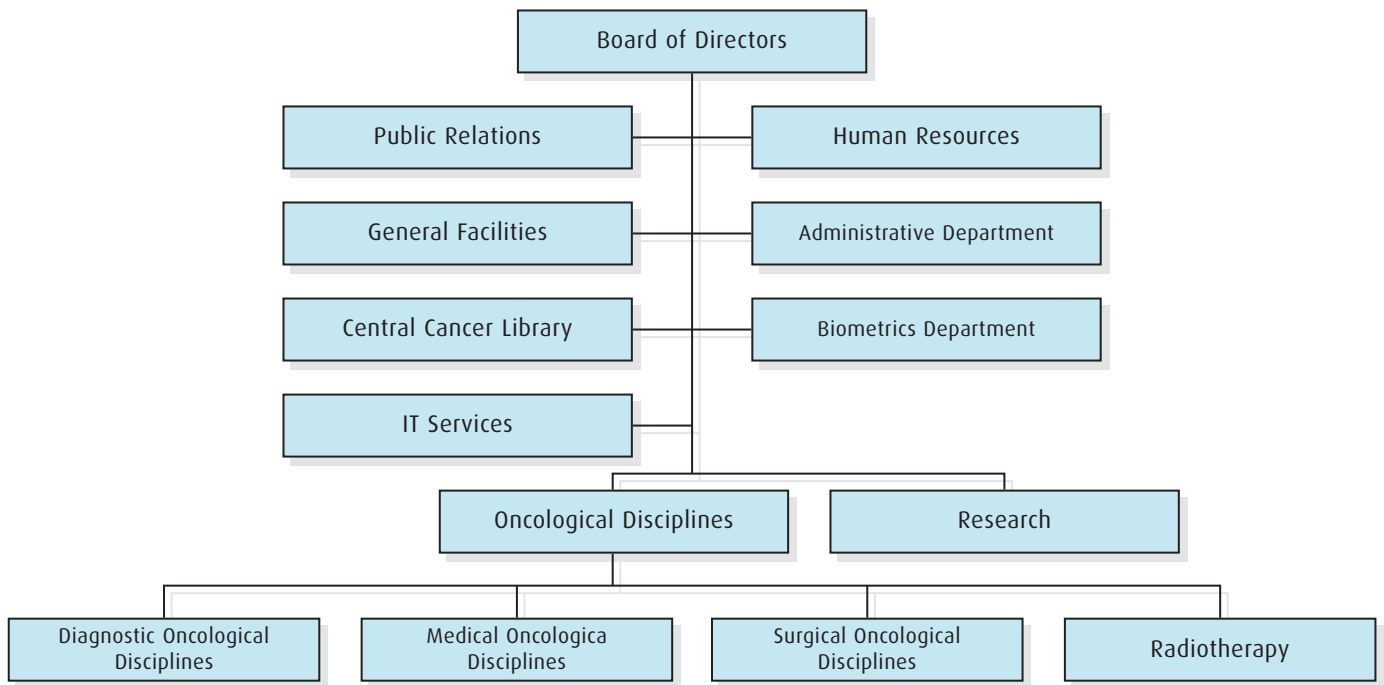
- Diagnostic Oncological Disciplines (DOD)
- Surgical Oncological Disciplines (Dutch abbreviation HOD)
- Medical Oncological Disciplines (MOD)
- Radiotherapy
- Research

These divisions receive support from central services, staff departments, the central cancer library, information technology (IT) services, the administrative department, human resources, public relations and biometrics.

Information about the day-to-day activity of the NKI-AVL:
Average staffing levels at the NKI-AVL

Organisational division	Number of employees
• MOD, HOD and DOD	804
• Radiotherapy	240
• Research	439
• Staff departments	356
Total	1848 (of which 1575 full-time)





Facts and figures about the clinic (2005)	Numbers
number of beds	180
daycare beds	30
operating theatres	5
irradiation units	9
consultation units in outpatient clinic	41
outpatient clinic visits	89,599
second opinions	1536
surgical activity clinic	11,010
surgical activity outpatient clinic	6,625
admissions	6,218
number of daycare patients	6,020
total number of care days	41,565
average treatment duration	6,7 days
mega volt therapy (radiotherapy)	3,947
brachytherapy	160
outpatient clinic chemotherapy	9,451
number of specialists	53
number of radiotherapists	24

Facts and figures about research (2005)	Numbers
clinical research divisions	4
fundamental research divisions	9
independent group leaders in fundamental research divisions	34
professors	28
scientific publications in 2005, in journals with an impact factor of 10 or higher	52
PhD theses	17
overall impact of publications in 2005	2,133
citations of publications in 2003	5,240

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History

The story of the NKI-AVL began in 1913, the year in which the first discussions took place about the establishment of an institute where 'patients suffering from malignant growths' could be treated. It was the brainchild of J. Rotgans, professor of surgery, publisher J.H. de Bussy and professor of pathology W. M. de Vries, all from Amsterdam. From the start, they insisted that the institute should also have facilities for 'a special study of cancer and related diseases'.

The inaugural meeting of the Association for the Netherlands Cancer Institute, which was held on 10 October 1913, was attended by prominent figures from the medical world and from Amsterdam society. An ambitious fundraising campaign was launched, regional committees were set up all over the Netherlands and Prof Rotgans set off on a tour of the country, to address these committees and to communicate to them his enthusiasm for the project. He did so with enormous success: within eight months, 315,000 guilders (142,940 euro) had been raised for the association – a huge sum in those days.

Some of the money was invested in a temporary site for the institute at 206 Keizersgracht in Amsterdam, which was called the 'Antoni van Leeuwenhoek Huis'. The clinic had room for 17 patients, while the laboratory could accommodate up to 10 workers. Cooperation between the laboratory and clinic was given a high priority even then, and the heads of both departments received written instructions to work together as closely as possible. The multidisciplinary





nature of the treatment offered was also evident from day one, with all information on a given patient being stored in a single file.

New fields of research began to be explored in 1916. In the clinic, attempts were made to treat patients with chemotherapy, while scientists in the laboratory began working on culturing human tumour tissue *in vitro*. Immunological studies were also carried out. The number of clinical and outpatient clinical irradiations grew steadily. The institute's first international meeting, held in 1922, was attended by 13 Dutch and 10 foreign scientists, and it has always seen cooperation with cancer scientists both in the Netherlands and abroad as an essential prerequisite for keeping abreast of the latest developments in oncology.

The structure and organisation of both the clinic and the research laboratory underwent many changes after the tumultuous years of World War II. Both the size of the management team and the number of scientific departments grew. New clinical departments were added

– surgery, radiotherapy, internal medicine, ear, nose and throat, gynaecology and clinical chemistry – but separate wards corresponding to these various disciplines were not created, because it was considered important to maintain the multidisciplinary approach to treatment. Shortage of space has been a recurring theme in the institute's annual reports since it was established. As a result of the explosive increase in demand for clinical and outpatient clinical irradiation, extra space had to be rented: first, temporarily, on the Rokin, and later (from 1 May 1917) at 1011 Prinsengracht, Amsterdam, where two new irradiation units were installed. In 1929, the institute moved into the old military hospital on the Sarphatistraat. In 1959, the decision was made to build a new institute at the present location on the Plesmanlaan in Amsterdam, and this was opened in 1973. Construction of the new laboratory building started in 1976, and was completed in 1979. The decision to build a new hospital next to the old one was taken in 2001, and the new building became operational in September 2003.







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