KOELIS, an expert in prostate diseases and a pioneer in the targeted management of prostate cancer

Press Kit

September 2023

KOELIS
Advancing Prostate Care

Contents

Working towards personalised management of prostate cancer diagnosis and treatment

From the past...

1 in 8 men will develop prostate cancer. Prostate cancer is one of the four most common cancers in the world. In 2020, 1.41 million new cases were recorded, including 375,304[1] deaths from prostate cancer.

In France, with 59,885 new cases and 8,100 deaths in 2018, prostate cancer accounts for 24% of cancers in men and ranks 3rd among deaths from cancer in men. It is rare before the age of 50, but its incidence increases progressively with age. This cancer has a good prognosis, with a 5-year survival rate of 93%[2].
Its management is mostly based on detecting cancerous lesions early and accurately. It confirms the presence or absence of cancer and establishes the prognosis, based on the size and aggressiveness of the tumours.

In most cases, a digital rectal examination, a PSA (Prostate Specific Antigen) assay and an MRI scan are performed one after the other so that the urological surgeon can make a diagnosis and consider a biopsy to dispel or confirm any doubts. Although imaging developments have helped reduce over-diagnosis and over-treatment, "conventional" biopsy, guided by endorectal ultrasound, has not demonstrated its ability to visualise and describe cancerous lesions. Its detection and qualification capacities are quite poor. Endorectal biopsies also present a non-negligible risk of infection (up to 17.5%)[3].

The main methods of treating prostate cancer are radiotherapy and hormone therapy, but even more so radical surgery (prostatectomy), which involves the complete removal of the prostate, and can at times have a significant impact on the patient's quality of life: 50% risk of loss of sexual function and 30% risk of incontinence.

... to the present

New MRI and ultrasound image fusion technologies are developing quickly, giving patients a precise diagnosis and personalised treatment. They help the urologist to assess the size of the tumour, to precisely remove the tissue from the cancerous lesions and determine the aggressiveness and severity of the cancer. Patients can therefore be offered personalised treatment with active monitoring, focal treatments or surgery.

Focal treatments use technology such as lasers, cryotherapy, irreversible electroporation and high-intensity focal ultrasound (see p. 13 for details). These techniques destroy the cancerous lesion from within, spare healthy tissue and reduce the risk of side effects such as impotence or incontinence that can occur during the disease and prostate removal.

(1) https://gco.iarc.fr/today/data/factsheets/cancers/27-Prostate-fact-sheet.pdf
(2) https://www.e-cancer.fr/Professionnels-de-sante/Les-chiffres-du-cancer-en-France/Epidemiologie-des-cancers/Les-cancers-les-plus-frequents/Cancer-de-la-prostate
(3) Ehdaie B., Vertosick E., Spaliviero M., Giallo-Uvino A., Taur Y., O'Sullivan M., et al. The impact of repeat biopsies on infectious complications in men with prostate cancer on active surveillance. J Urol. 2014 Mar; 191(3):660-4.

1. KOELIS, a MedTech pioneer in Grenoble and leader in 3D image fusion

The company is a member of both the Minalogic and Lyon Biopôle competitiveness units, as well as the Medicalps network in Grenoble, and has been awarded the French Tech and BPI excellence labels (winner of BPI France's global innovation competition in the "Individualised Medicine" category in 2019).
KOELIS is an innovative SME based in Grenoble, that has been paving the way for personalised medicine in prostate cancer since it was founded in 2006.

Click here to see the video

1.1 Developing an innovative imaging platform for the diagnosis and targeted treatment of prostate cancer

KOELIS has developed a 3D image fusion system for personalised management of prostate cancer. This platform, named Koelis Trinity®, is based on disruptive innovation combining 3D ultrasound and image fusion technologies. Clinicians can use this platform to visualise the prostate in real time and create a 3D map by recording the lesions identified. It also guides diagnostic or treatment needles with great precision into the targeted areas. The innovations developed by KOELIS are based on applied research, previously conducted with the University of Grenoble (TIMC-UJF), the Pitié-Salpêtrière teaching hospitals in Paris and Grenoble and, more recently, with the robotics laboratory in Paris (UPMC-ISIR).

« Koelis is a specialist in prostate diseases. The innovative technologies that we develop are already being used to diagnose and treat cancer. We aim to provide doctors with the highest level of precision and versatility, and patients with the greatest possible safety and quality of life. »

states Antoine Leroy, Chairman, CEO and co-founder of KOELIS.

1.2 "Made in France" design and production with international recognition

KOELIS has always combined clinical research with technical performance, software and ultrasound development, French manufacturing and international deployment.
Its registered office, clinical research department, all of its innovation departments (R&D, Research, Medical Software Application and Electro-Medical Devices), and its production site are all located in Meylan (38 - Isère).

KOELIS uses French and European suppliers and contractors to design and manufacture its surgical workstations, 3D imaging probes, accessories and light robotic equipment. Its software is entirely designed and developed by its engineers, PhD students from leading universities and experts in prostate diseases.

With regard to its commercial side, KOELIS has three international subsidiaries located in the United States, Singapore and Germany. Its products are sold in 50 countries across the world and are distributed through around forty distributors in Europe, Africa, North America, South America and Asia.

1. KOELIS, a MedTech pioneer in Grenoble and leader in 3D image fusion

1.3 Development supported by specialist healthcare investment funds

Innovahealth partners, the leading private equity firm specialising in the growth of medical devices, acquired a majority stake in KOELIS in 2019. InnovaHealth is based in the United States and has around $200 million under management and over 100 years' experience in investments in the global medical device market.
Medevice, which is a French investment fund that specialises in medical technologies and was KOELIS' chosen operational and financial partner from 2012 to 2019, is still a shareholder.

Key figures

11 million
euros in sales in 2022
(+40% compared with 2021)

100
employees

A distribution network in
50 countries

500 Trinity® medical platforms
sold worldwide to date;
80 centres in France are using them

½ million patients
across the world have benefited from the KOELIS prostate cancer detection system

1.4 The key stages in the history of a start-up that has become an international company

2001
Antoine Leroy and Patrick Henri met at PRAXIM, a company specialising in computer-assisted surgery in the field of orthopaedics.

2006
KOELIS SAS was created in Grenoble.

2009
Urostation® was launched as a software platform for prostate biopsy mapping, based on 3D images and patented algorithms.

2011
KOELIS raises a million euros from Medevice investment funds.

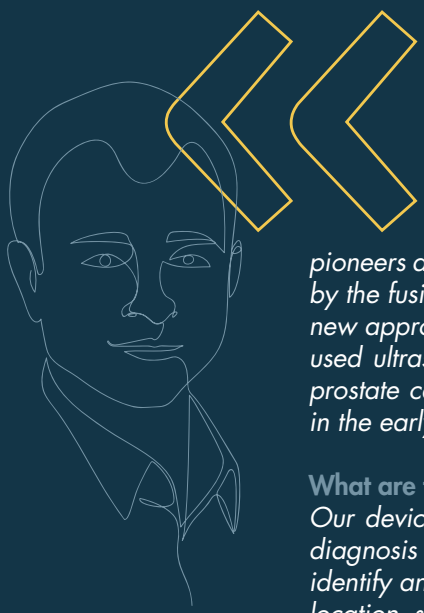
2015
KOELIS Inc was created in Princetown, United States; Trinity® was launched as the first integrated 3D imaging platform for prostate mapping and targeted prostate surgery.

2016
A new application for transperineal biopsy was launched.

2019
The innovahealth investment fund acquired a stake in the company; KOELIS Singapore was created.

2022
KOELIS Germany was created.

Three questions for Antoine Leroy, Chairman, CEO and co-founder of KOELIS



Can you tell us what makes KOELIS unique?

Koelis is a fast-growing, innovative company that is proud to represent French tech on the international stage. We do not place ourselves in the medical imaging sector, but rather in the innovation market. We are pioneers and leaders in innovative prostate mapping for guided prostate cancer surgery, by the fusion of proprietary 3D imaging disruptive innovation and robotics. We have a new approach compared to what is currently on the market. Until recently, all urologists used ultrasound for diagnostic consultations. We are helping to meet the challenges prostate cancer treatment, which affect over a million patients worldwide, particularly in the early stages.

What are the benefits of the KOELIS devices approach for patients?

Our device provides precise, reliable images, so patients can benefit from illustrated diagnosis and personalised care with active monitoring and targeted interventions to identify and treat significant lesions, in a potentially shorter time. The patient knows the location, shape and position of the lesions in his prostate. Having this information makes a big difference. It forms the basis of the discussion with the doctor, in order to decipher and plan the most suitable treatment, with the main aim of preserving quality of life by avoiding radical surgery.

What are the advantages of these devices for the practitioner?

Koelis' contribution to practitioners is both substantial and undeniable. We provide the vision: on their screen, they can see what they're doing as they do it. Our system also guides the needle with millimetre precision, infinitely more precise than with a conventional ultrasound scanner. Finally, our device stores images of the prostate at each stage of biopsy and treatment, so we can monitor the development of the lesions and personalise treatment. I should also note that scientific societies, such as the European Association of Urology, are using the results of our clinical studies to update their recommendations.

2. Innovations in targeted treatment of prostate cancer

2.1 Seven patent families used on the management system for diagnosis, active monitoring and targeted treatment

The KOELIS strategy is to offer a targeted diagnosis and focal treatment for cancers with a medium risk, as an alternative to active surveillance and radical treatments.
The successive major innovations developed by KOELIS within its Trinity platform® are used to:

- provide a solution for mapping and guiding diagnostic biopsies,
- provide a planning and guidance solution for existing focal treatment methods (universal tool),
- offer an innovative, ultra-targeted approach using a needle of the same size as the biopsy needle, which can be guided in the same way and with the same precision, wherever the lesion is located.

The platform's approach and capacities allow practitioners to direct patients to:

- active monitoring, which consists of repeating screening and diagnostic procedures over time, focusing on the known lesion(s), with the aim of monitoring any progression
- potential focal treatment
- radical treatment (surgery, radiotherapy) if necessary

The Trinity® platform incorporates seven patent families developed by KOELIS and is based on the following technologies:

- **three-dimensional ultrasound, known as "full 3D"**, which automatically navigates around the organ with millimetric precision.
- **3D medical image fusion algorithms,** "elastic" fusion, which takes into account the deformations of the organ to display precise information about the target within the space.
- **Organ-Based Tracking Fusion™ (OBT Fusion™)** is a unique, patented solution that compensates for patient movement and maintains image fusion throughout surgery.

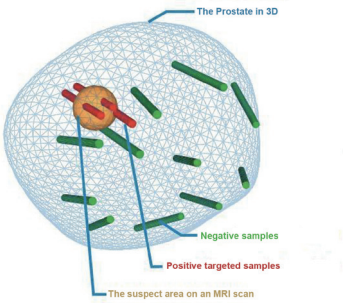
2.2 3D imaging using elastic image fusion, major technological progress

It has been demonstrated and proven by Scientific Societies that an MRI scan, as a first line of defence, enables the potentially cancerous lesion(s) in the prostate to be precisely located. Therefore, by combining MRI and ultrasound images - known as image fusion - the urologist can take biopsies within the lesion or lesions identified, with the aim of offering a suitable and progressive treatment depending on the lesion.

There are currently two image fusion methods:

- cognitive fusion: this is carried out cognitively without any technological assistance. The urologist looks at the MRI images supplied by the radiologist, and uses the ultrasound image to determine where they will perform their biopsies.
- rigid fusion: this is produced by superimposing MRI and ultrasound images in a crude and unadjusted way. The images are then distorted to fit together and are not sufficiently accurate.

2. Innovations in targeted treatment of prostate cancer



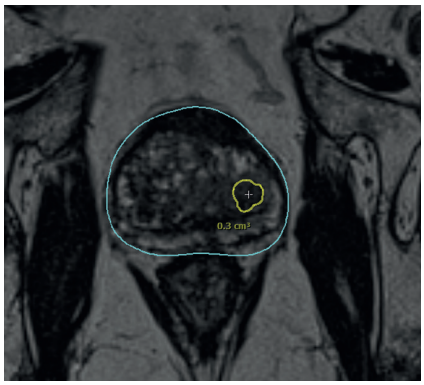
This major innovation developed by KOELIS, Organ-Based Tracking (OBT), is based on elastic image fusion. Its computer technology is based on the principle of rigid fusion and uses algorithms to precisely superimpose the MRI image used for identifying lesions and the ultrasound image that provides a real-time image of the prostate.
The merged data provides a 3D map of the prostate, which is modelled and reveals any suspicious lesions in real time.

2.3 Close-up of the key stages of a typical targeted biopsy protocol using 3D image fusion

A biopsy using the Trinity® platform is performed as follows (see figures below):

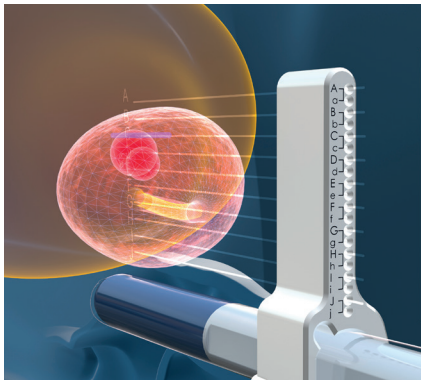
STAGE 1

The radiologist defines the areas of interest on the MRI image (in blue on the photo).



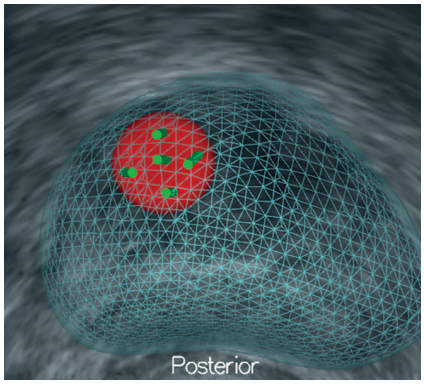
STAGE 2

The urologist imports the radiological data directly from the Koelis Trinity® platform and merges it with the live ultrasound image of the patient lying down. It uses the Koelis Trinity® interface to guide the biopsy needle to the suspected area (on the photo: the 3D ultrasound probe, the prostate, the needle guide, the needle and its target, for a transperineal approach).



STAGE 3

All sampling locations are recorded in the map; it shows that the 3 biopsies in the target contain cancer cells (red samples in the photo).



During an operation, the practitioner checks the ultrasound image on Trinity's® large touch screen. It appears in real time on the right side of the screen. The 3D map appears on the left side of the screen as you explore.

2. Innovations in targeted treatment of prostate cancer

Opposite is the final result of a standard protocol of 12 equally distributed samples, plus 2 samples in the MRI target (in red on the right). The practitioner sees, targets and records their biopsies, which can then be compared during follow-up biopsies if the patient is put under active monitoring.

2.4 From biopsy to targeted treatment using 3D image fusion

The Trinity® platform allows the practitioner to offer a choice of non-invasive and non-radical treatments, using 3D imaging and millimetric needle guidance, carried out in total confidence in less than an hour in the consultation room or in the operating theatre through the transrectal or transperineal route, which is now recommended (see below):

- Fibre laser technology: a needle that uses heat to destroy cancer cells in a focused way, thereby preserving other healthy tissues.
- Cryoablation systems: a needle that destroys cancer cells by intensely reducing their temperature, thereby preserving other tissues in the organ.

Techniques in the evaluation phase:

- Irreversible Electroporation (IRE): a needle that delivers a high-voltage, low-intensity current, without thermal variation, to destroy cancer cells.
- High Intensity Focal Ultrasound (HIFU): a needle that delivers high-intensity focal ultrasound to destroy cancer cells using heat, without damaging the surrounding tissue.
- Targeted Microwaves Ablation (TMA): a needle that delivers targeted microwaves to destroy cancer cells using heat, without damaging the surrounding tissue. This approach is the subject of clinical research by KOELIS (see p. 10).

These targeted prostate treatments (local ablation or hemi-ablation) mean that patients can maintain their quality of life, mainly because urination and sexual function are preserved. The prostate can therefore be fully removed only in the most critical situations.

Transperineal biopsy and targeted treatment: a major innovation for patient comfort and safety

Biopsies and targeted treatments of the prostate can be carried out transrectally or transperineally. The transrectal route has recently been questioned because of its high risk of infection (up to 17.5%)[4].

KOELIS has been offering tools for transperineal biopsies since 2016.
This innovative, painless technique passes through the skin via the perineum instead of through the rectum to take samples of prostate tissue. The infection rate is almost zero, as are all the other possible complications. This approach can be performed under local anaesthetic on an outpatient basis, which also reduces patient anxiety about the examination and improves their comfort.

(4) Ehdaie B., Vertosick E., Spaliviero M., Giallo-Uvino A., Taur Y., O'Sullivan M., et al. The impact of repeat biopsies on infectious complications in men with prostate cancer on active surveillance. J Urol. 2014 Mar; 191(3):660-4.

3. Clinical research programmes on the targeted treatment of medium-grade prostate cancer using a microwave needle

The effectiveness of KOELIS technology has now been proven by a corpus of over 60 international clinical publications that demonstrate the feasibility and benefit of combining mapping and image fusion for a more accurate, personalised diagnosis. These data have led to changes in European guidelines. Since its creation, KOELIS has been undertaking clinical research programmes. Several studies have validated its approach to diagnosing prostate cancer and supported the development of its new transperineal biopsy technique. A number of clinical trials are now being conducted to assess the safety and performance of the TMA (Targeted Microwave Ablation) therapeutic proposal.

« Koelis is clearly committed to clinical research, and its strategy is based on ethical and scientific choices. The multicentre Violette study we are carrying out is an example of this, with 65 patients already recruited and 100 patients having undergone an operation. Microwave treatment needles already have CE marking so that we could market them. but we want to assess their efficacy through clinical trials. This approach is ultimately a gamble, but is very representative of our corporate strategy, which is geared towards scientific transparency. »

states Claire Jossan, Head of Clinical Research at KOELIS.

3.1 FOSTINE, the single-centre feasibility, safety and efficacy studies for interventional, non-surgical treatment of tumours directly within the prostate

Specific features of the FOSTINE study

FOSTINE covers feasibility and efficacy studies 6 months after non-surgical interventional treatment of prostate cancer:

- Single-centre studies
- The hospital is a sponsor
- KOELIS provides financial support
- 62 patients underwent an operation in total

The first FOSTINE clinical study began with a feasibility trial at Cochin Hospital (75 - Paris) in which 10 patients were included and monitored for 6 months, between 2017 and 2019. Its main objective was to assess and validate the feasibility and the accuracy of a non-surgical outpatient interventional treatment technique that involved directly targeting the tumour in the prostate, while preserving healthy tissue, using the unique and innovative technologies developed by KOELIS.

In this study, the treatment was performed by inserting a fine needle guided by image fusion into the tumour target, where microwaves were then delivered to destroy the tumour. This minimally invasive approach aims to treat small tumours quickly, while reducing the risk of functional complications.
The procedure proved feasible for 80% of patients. For 8 out of 10 patients, complete coverage of the target area was visible on an MRI on day 7. In addition, no serious side events were reported for the entire cohort. Patients reported no post-operative pain and there was no change in functional scores observed.

3. Clinical research programmes on the targeted treatment of medium-grade prostate cancer using a microwave needle

Three other studies are still underway:

A **Fostine Turin (transperineal route)[5]:** there were no serious adverse events (SAEs) or post-operative pain for the 11 patients included in this study. No changes were observed in functional scores (urinary and sexual).

B **Fostine Hong-Kong (transperineal)[6]:** preliminary results on the first 15 patients treated have already been published. In this study, the investigator has the option of treating several lesions per patient. Therefore, the first 15 patients operated on correspond to 23 areas treated. This is the first article to present efficacy results. This is assessed through targeted biopsies in the treated area carried out 6 months after the operation. 91.3% of biopsies taken from the 23 treated areas were free from cancer at 6 months of follow-up. Additionally, these preliminary results once again highlight that there were no serious adverse events, and that patients' functional scores and quality of life were preserved.

C **Fostine Brussels (transrectal route):** results have not yet been published (11 patients included).

3.2 The VIOLETTE study, a phase 2 clinical trial[7] to assess the efficacy of focal microwave ablation guided by 3D image fusion for medium-risk prostate cancer.

The VIOLETTE study is a phase 2 multicentre clinical trial following on from the first single-centre trials. It assesses the efficacy of focal ablation in prostate cancer guided by 3D image fusion.
The primary endpoint is for the treated area to be free from cancer 12 months after treatment. Quality of life and patient satisfaction are among the secondary endpoints, as is the assessment of functional scores (urinary and sexual). MRIs are also carried out during patient follow-up, which ends with the biopsies performed at 12 months.
The protocol was designed in accordance with the latest international recommendations[8] and the FDA[9].

Specific features of the VIOLETTE study:

Re.: study on the efficacy of focal ablation in prostate cancer guided by image fusion
- prospective multicentre interventional non-comparative study carried out in 7 European centres (including 6 in France)
- KOELIS is in charge of the study and is the sponsor
- 65 patients included in the different centres, treated in two different ways (transperineal route / transrectal route)

Professor Nicolas Barry Delongchamps, Professor of Urology at Hôpital Cochin, is the Co-ordinating Investigator of the VIOLETTE study.
The first intermediate results from VIOLETTE on the 20 patients treated with 6 months follow-up are expected in 2023.

(5) Oderda et al., Eur Urol, October 2022
(6) Chiu et al., PCAN, July 2022
(7) NCT04582656
(8) Lebastchi et al. – Eur Urol 2020 - Standardized Nomenclature and Surveillance Methodologies After Focal Therapy and Partial Gland Ablation for Localized Prostate Cancer: An International Multidisciplinary Consensus
(9) Recommandations de la FDA sur les investigations cliniques relatives aux dispositifs d'ablation de la prostate : https://www.fda.gov/regulatory-information/search-fda-guidance-documents/clinical-investigations-prostate-tissue- ablation-devices

Annexes

Research and innovation at KOELIS

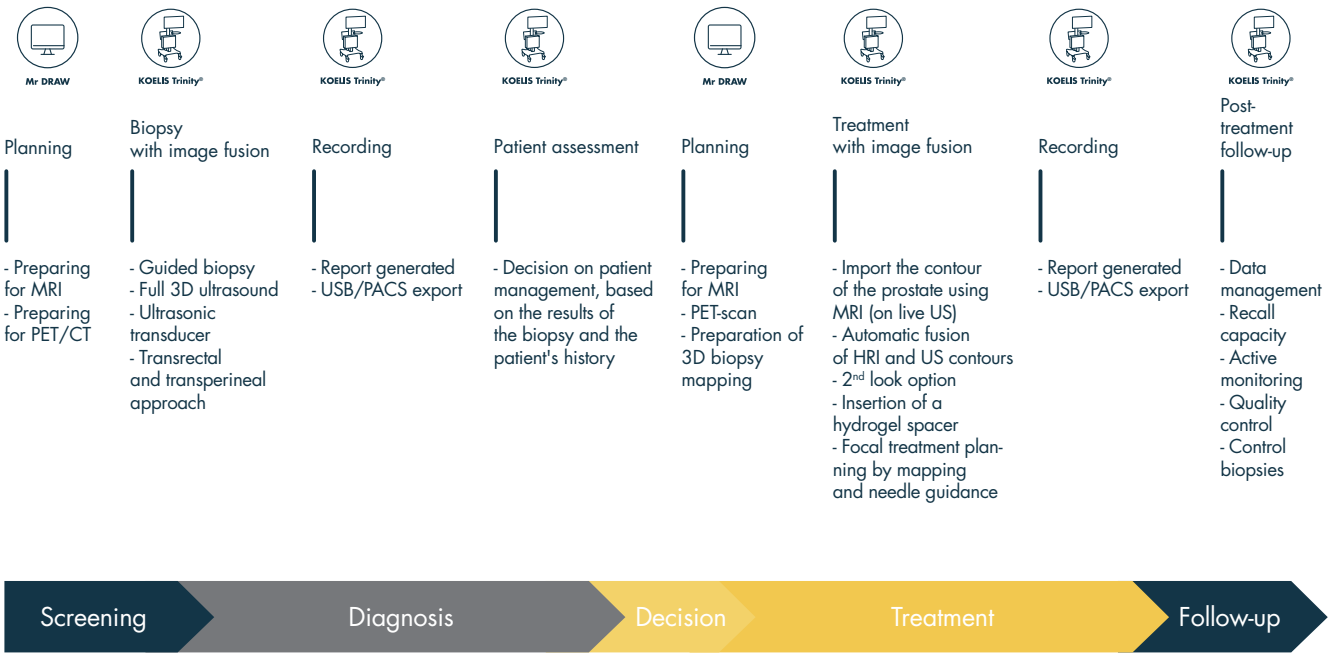
All KOELIS R&D activities, which are also centralised at the registered office, are organised in close collaboration with the marketing, industrialisation and regulatory departments. They include 22 employees, including specialist engineers who work on the design of new products, from development through to production and support (testing technical solutions, sourcing components, writing specifications, etc.).

It is organised into 3 distinct divisions:

Annexes

The KOELIS personalised prostate cancer treatment system

From fusion biopsy to active monitoring and treatment of the prostate throughout the patient's life.



Annexes

Data about prostate cancer in France[10]

Prostate cancer accounts for 25% of cancers in men. It is rare before the age of 50, but its incidence increases progressively with age. This cancer has a good, or even very good prognosis, with a 5-year survival rate of over 90%.

Key figures

50,400
new cases in 2015 in mainland France

68 years old
Median age at diagnosis in 2018

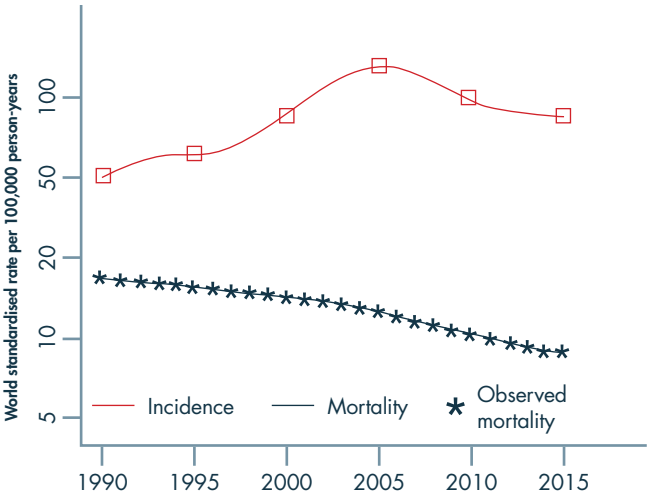
Prevalence estimated at
643,156
people in 2017

8,100
deaths in 2018, down 3.7% per year between 2010 and 2018

83 years old
Median age at death

Net survival standardised by age
at 5 years: **93 %** (stable); at 10 years: **80 %**

Incidence and mortality rate for prostate cancer in France by year (1990-2015)



Source: National estimates of cancer incidence and mortality in metropolitan France between 1990 and 2018 Volume 1 - Solid tumours.

This cancer ranks 3rd among deaths from cancer in men. Mortality has been decreasing regularly since 1990. This is partially due to improved treatments, particularly those for advanced cancers, and to access to prostate cancer screening, which enables them to be diagnosed at an early stage: 80% of cancers are diagnosed while still localised in the prostate, but the main prognostic factor for this cancer is the stage at diagnosis.

(10) E-cancer

KOELIS
Advancing Prostate Care

koelis.com

Press contact:

Marjorie Castoriadis
Tel. : 00 33 6 11 21 44 89
marjorie.castoriadis@prpa.fr

Thomas Martins Pinheiro
Tel. : 00 33 7 88 31 16 48
thomas.martins-pinheiro@koelis.com

22 chemin du Vieux Chêne
38240 Meylan - France

KOELIS SAS - Registered office: 22 chemin du Vieux Chêne - 38240 Meylan - France - Grenoble Trade and Companies Register B 492 218 375
Simplified joint stock company with share capital of €1,190,900 - SIRET business no.: 492 218 375 000 29 - APE trade sector code: 7112B