

Category

Best Medical Technology

Drug / Device Name

Papillon system

Compound/ Tech Name

Radiotherapy device

Trade Name

ARIANE CLERAD

Date of Approval

2021-06-15

Indications

Rectal cancer

Therapeutic Categories

Radiotherapy

Attached Files:

- papillon Plus Clerad 2023.pdf

Background information and need for drug/device

Cancer is the number one killer in most of the world countries. When treated at an early stage a long term cure of cancer is possible in 50% of patients. For exemple in France or UK one person out of three will develop during his life one (or two) cancers and one out of four will die from cancer. In France every year 300 000 new persons will be diagnosed with cancer and 150 000 will die from cancer (out of 600 000 deaths per year. The main treatment of solid tumours is surgery and the main tretament of leukemia or lymphoma (cancer of lymph nodes) is chemo-immunotherapy. The third main treatment of cancer is radiotherapy (RT) which is given to one cancer patient out of two. Radiotherapy has three main virtues, the S C : 1) Curative treatment, with half of cured patients receiving some form of RT. 2) Conservative treatment : It is thanks to RT that, when affected with cancer, we can save (or preserved) organ like eye, larynx, breast, anus, bladder and limb. Mutilating surgey can be avoided using RT in such tumour site. 3) Cost-effective treatment because RT all included represents only 10% of the total cost of cancer for a country.

This new radiotherapy device (Papillon) which is presented here, is a RT machine co- manufacturd in UK (Ariane medical systems) and France (Clerad). It is a unique technique of irradiation called Contact X-ray Brachytherapy (CXB). This system is delivering a soft x-ray beam of 50 kVp with a high dose rate (15 Gy/ mn) in a small volume (5 cm³). The clinical consequence is high cure rate of tumour and low toxicity. It is a simple ambulatory treatment dedicated to control small accessible cancers. Since many decades it is used to treat early skin tumours and eyelid carcinoma. Combined with surgery it can cure small breast dancer using an intraoperative strategy.

This technique was pioneered in the 1970s in France to treat early rectal cancer but the scientific proof of its benefit was lacking. An European randomised control trial (OPERA) recently published in the prestigious medical journal Lancet is now bringing high level evidence that CXB can cure early rectal cancer without any surgery and preserve a normal bowel (rectum).

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- CV JPG Anglais 28-3-23.pdf

History of the development of the drug/device

Radiotherapy using soft x-rays 50 kVp was at the origin of radiotherapy in the early 1900s. A first machine was manufactured by Siemens in the 1920s. After the second world war the Philips RT 50 unit was very popular and in France, 100 machines in the 1970s were in regular use especially to treat skin tumours. In Lyon, Pr Jean Papillon (1914-1993) a radiation Oncologist working in the cancer Center Léon Bérard, was able to adapt the Philips machine to treat rectal cancer through an endocavitary approach using rigid rectoscopy and dedicated rectal applicators. I had (Pr JP Gérard) the chance to learn the technique with Pr Papillon during 15 years of close collaboration in Lyon. When I moved to Nice to become General Director of the Cancer Center Antoine Lacassagne, I transferred the technique and a Philips unit to Nice. Unfortunately the machine was old and I was obliged by ASN (safety Nuclear authority) to stop it. With the upcoming of modern linear accelerators the Philips company was not anymore manufacturing this RT 50. By chance, in 2004 I met a British engineer (K Spanswick) and together we succeeded to manufacture a new CXB machine that we called Papillon (P50tm). This was celebrated as a Renaissance of the Contact X-ray Brachytherapy. The two first P50 were acquired in 2009 by me (JPG) in Nice and by Pr A Sun Mynt (in Clatterbridge- Liverpool) who has been trained by me in Lyon in 1994. Both together we developed the ICONE network of P50 users in France (3 machines plus one installed recently in Paris, Institut Gustave Roussy), UK (4 machines) and Switzerland (1 machine). In France we were able to publish our results in the treatment of early rectal cancers and we demonstrated that a planned organ preservation was possible in 84% of cases using a combination of CXB and chemoradiotherapy. Similar results were also presented by the British teams. To bring the scientific proof of the benefit of this CXB treatment we set-up the OPERA (Organ Preservation Early Rectal Adenocarcinoma) randomised control trial. This trial was conducted in France, UK and Switzerland between 2015 and 2020 and accrued 141 patients. The results published recently in Lancet showed that at 3-year follow-up it is possible to achieve 81% of organ preservation using CXB and even 97% when treating tumours smaller than 3 cm. H Rutten a surgeon from Eindhoven wrote an editorial in Lancet to comment this study saying : It is the first randomized trial bringing a high level of evidence for the possibility to cure early rectal cancer using CXB with a good bowel function. These results should lead to a change in practice.

During the same period of time, a new Papillon unit (P+ tm) was designed to perform breast IORT (Intra operative RadioTherapy). The first patients were treated in Centre Antoine Lacassagne (Nice) in 2018 and the results published in 2023 showed that in a series of 26 patients a local excision for small breast cancers in women over 60 years with an IORT using P+ and delivering 20 Gy in one minute during the surgery time, provided local control and breast preservation in all the patients.

Both P50 and P+ are used to treat regularly skin and eyelid small carcinomas with excellent results.

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- Galien.ppt

Why this drug or device is innovative, the broad implications for future research, and/or how it will improve the human condition

The P+tm machine with a CE mark granted to Clerad company is presently the main device offered to the market in Europe and UK to perform CXB treatment for three main types of cancer : rectum, skin and breast.

1) Generally speaking, this CXB using the P+ machine is a simple treatment usually performed on an ambulatory bases. As it irradiates only a very small volume the tolerance is always good and as the dose is very high and delivered very accurately under eye guidance the efficacy is very good. It is the only radiotherapy device with such a high dose rate of 15 Gy/ minute which makes the treatment time very short (one or two minutes). This short treatment time makes possible the use of CXB to treat through an endoscopic approach rectal cancer. It is the only technique delivering the dose in one minute during breast IORT (vs 30 minutes for other 50 kV machines). From an economic point of view this system is very cost-effective. The Price of a P+ is around 500 000 Euros and the machine can work for 10-13 years. In France the cost of a rectal treatment is 3 000 Euros. It is 800 Euros for skin and 1000 euros for breast treatment. From a radioprotection point of view the system is very safe, working on battery with little shielding (soft x rays) and no radioactive element which is a model for sustained development.

2) From a clinical point of view this unique systems provide excellent and original results. For the first time using the Papillon technique it is proven that early rectal cancer at any age and in fully operable patient can be treated and cured without any mutilating surgery which is a tremendous benefit from a quality of life perspective. For the first time breast IORT can be performed with only one minute of irradiation in a one day treatment for early breast tumours especially in women above 60 years of age which is a huge gain of simplicity and comfort. For skin cancers the results are excellent and the technique is privileged in elderly, frail patients. Future developments are expected in the field of urologic, gynecologic and head and neck cancers. In rectal cancer randomized trials are ongoing, in France and Netherland to test the use of CXB in more advanced tumours.

Attached Files:

- Why 3.docx

Please provide appropriate references (ie Pubmed links)

Lancet Gastroenterol 2023

CTRO 2023

Attached Files:

- Rutten2023_LancetGastroenterolHeptol.pdf