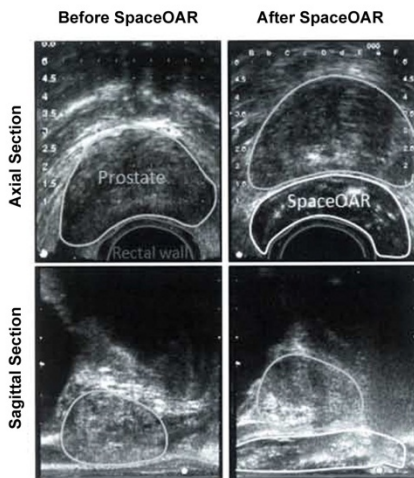




Medical specialists azM MAASTRO, left to right: Tom Tuytten, middle Francis van Gils and far right Kees van de Beek

Prostate cancer treatment improving through *optimized collaboration*



MAASTRO clinic is an independent institute for radiotherapy, situated adjacent to the university hospital of Maastricht (azM). In Limburg a close collaborative relationship exists between the MAASTRO clinic and several area hospitals for the treatment of prostate cancer. When it comes down to collaborating with urologists, MAASTRO clinic performs a central function in a web of several partnering hospitals from Maastricht, Heerlen, Sittard, Roermond, Weert and as of recent, Venlo as well. Patients qualified for and preferring surgery by means of the Da Vinci robotic procedure are in very well experienced hands at azM. Urologist Dr. Tuytten has performed several hundreds of procedures with the Da Vinci robot.

Open abdominal procedures are performed in Roermond, Heerlen and Venlo. The results have been good due to their expertise from many years. Nerve-sparing is an option as well. Much experience has also been obtained with brachytherapy; as of yet, more than 800 patients have been treated. This is done in close collaboration with the urologists. With the exception of Weert and Roermond, each hospital has an active specialty team consisting of a urologist, a radiation therapist, a physicist and a medical dosimetrist. Said close collaboration promotes and facilitates team deliberations. As a result, deliberations occur often, which is to the patient's benefit.

Gel pad

Once prostate cancer has been diagnosed, and the tumor is confined within the prostate, the patient is confronted with the difficult decision between radiation therapy and radical prostatectomy (surgical removal of the prostate). Less common therapies such as CRYO-therapy and HIFU-therapy are not being used as often yet and this sometimes complicates the decision.

Potential damage to the intestines is an important consideration in this, especially related to external radiation therapy.

Many investigators have been studying the subject of limiting or preventing intestinal damage during radiation therapy. In September 2008, the SCP already reported on the balloon technique, which makes it possible to shield the majority of the intestines from the field of radiation. The application of gold markers; improved imaging techniques (such as cone beam CT, 3D Ultrasound); modern planning techniques and sophisticated devices is constantly improving the quality of radiation treatments. As a result, side effects- specifically of the large intestine- are less frequent.

The search for perfection is still going full throttle. For the first time in The Netherlands, a patient was treated at MAASTRO clinic in Maastricht with a commercial version of the so-called gel pad (see text below by H. Kuipers). As of yet, three patients have received treatment with this. For the purpose of gaining experience with this, the company has provided ten free samples. After this pilot, an evaluation will be done to determine the most appropriate

individuals for this instrument and- also important- to determine allocation of costs. Due to the significant cost of this treatment, a cost-benefit analysis should be performed in order to convince healthcare providers.

On the other hand, prolonged follow-up for bleedings, possibly caused by colonoscopy, blood transfusions, additional doctor's visits, medication and hyperbaric oxygen therapy for severe bleedings are not inexpensive either.

In one session, Dr. van de Beek, urologist at azM, injected a gel-like substance while simultaneously placing gold markers. These 2 components will converge in the tissue and "stiffen up" into a hydrogel which is injected between the intestinal wall and the prostate. An ultrasound probe (as used with brachytherapy) is inserted into the anus. This will provide a clear view of location and movements. The needle is inserted through the perineum (skin between anus and scrotum). The body steadily breaks down the material (polyethylene glycol). All material will be gone after approximately six months. It will remain in place during the radiation period of 7 to 8 weeks. By doing this, a space of at least 0.4 inches (1 cm) is created between the exterior of the large intestine and the prostate (see attached MRI-picture). Hardly any radiation enters the large intestine afterwards.

By reason and by evidence provided it is deduced that the occurrence of side effects is largely reduced with this method. This material has been known from experience since it is also being used in cosmetic surgery and orthopedic surgery, among other areas.

Dr. van Gils, radiation therapist at the MAASTRO clinic in Maastricht, was asked about her experiences with this technique.

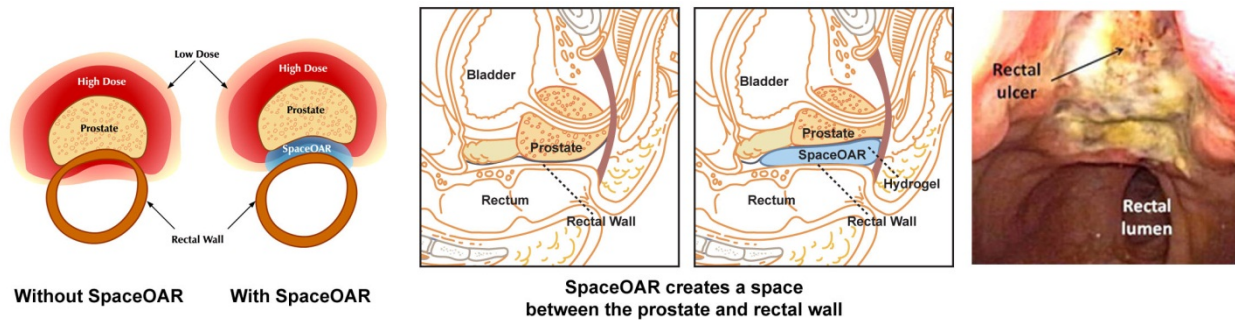
Dr. van Gils: In Europe, mainly in Belgium and Germany, approximately one hundred gel pads have been placed and here we have so far treated three patients with them. Once the gel is inserted at the appropriate location, a space of at least 0.4 inches (1 cm) is created between the intestinal wall and the prostate. This margin is wide enough to minimize damage to the colon, if any. Chances of having intestinal problems later on are smaller for the three patients who have been treated here. Until now, my colleagues in Belgium and Germany have been reporting similar positive experiences as well.

It seems pretty obvious; one could ask why this hasn't been thought of before?

Dr. van Gils: this technique can be applied to both external beam and internal beam radiation therapy, although there's still less risk of intestinal damage involved with brachytherapy compared to external beam radiotherapy.

A higher radiation dose is used with hypofractionated radiation therapy while cutting the number of radiation sessions in half. The treatment takes 7 or 8 weeks as well but radiation treatments are every other day rather than every day. This means less burden on patients, more effective use of radiation devices and as a result, cost-effectiveness. Does the additional safety of the gel technique render this method more favorable?

Dr. van Gils: this new method of radiation treatment definitely improves safety. Hypofractionating releases a higher radiation dose at a time. This basically increases the risk



Dr. van Gils: of course there have been thoughts in this direction before but finding the material that does not need to be inserted and then removed- a procedure that carries risks for complications- was fairly difficult. This gel is broken down and removed by body.

Can this technique be applied to brachytherapy as well?

of damaging normal tissues. The total dosage on the other hand is less. It is still being studied how this exactly relates to the traditional radiation methods. The results are not available as of yet. It needs to be stated that this hypofractionating method has not been explored in detail yet, but it's already being applied in certain places.

Is this technique expensive and what is the reimbursement policy of insurance companies?

Dr. van Gils: Ideally, this would be included into the DPC's in the future. Up until now, the manufacturer at no cost provided the gel that has been used. In the long run, the use of this gel with radiation therapy will be cost saving. In addition to the major improvement to quality of life, it will also prevent expensive treatments of intestinal and anal complaints in a number of cases. However, as usual, cost precedes quality. I hope everyone realizes this.

The story of Harm Kuipers' experience

At first, in the beginning of 2010, it appeared to be confined prostate cancer but an MRI pointed out that it had outgrown the prostate capsule and had also grown into several lymphatic nodes. The unfavorable Gleason score (8) precluded him for surgery and hormone therapy was initiated immediately. External radiotherapy of the prostate and lower abdomen was proposed. The price of possibly gaining more time with this treatment is the occurrence of side effects. One of the most dreaded side effects is rectal damage (the anus) – responsible for long term and sometimes even lifelong complaints from patients.

Being a medical doctor myself, I had found out that with patients who had elected this technique at UMC St.

Radboud in Nijmegen, the dose load on the rectum was being spread over a larger surface area when a small balloon had been inserted into the rectum prior to each radiation session.

The downside is that the anterior part of the rectum is thus being pushed into the radiation field. In any case, I preferred the balloon option to doing nothing at all, even though I realized that it increased the demands on the workers in the radiation therapy clinic, as insertion and removal of the balloon had to be performed at each session.

When I mentioned my wish for the balloon to doctor van Gils- radiation therapist- she told me she had something that was possibly even better and completely new. The hospital in Maastricht had obtained approval to apply a completely new technique, which appeared even better than the balloon. The new method consisted of inserting a gel between the prostate and the rectum, thus pushing the rectum further away from the prostate resulting in less exposure to radiation. The gel is made of a biological substance that is broken down by the body after completion of radiation. Immediately, I was convinced and without requiring time to rethink, I indicated that I wanted to use this technique. This was just a little too soon; it appeared that this technique was not being used yet in The Netherlands and formal approval had to be obtained first. It took several

months before I received an email stating that approval had been given and appointments could be made to insert the gel. This could be done simultaneously with insertion of the gold markers for radiation.

I was confident, even though I would be the first patient and the specialist did not have any experience with this. After all, my doctor, urologist dr. van de Beek, has ample experience with brachytherapy and the technique of inserting the rods has many similarities with inserting the gel.

Several people from the manufacturing company had flown over (one person even from the USA) to accompany the procedure since this was the first time for the urologist as well. Everything went just fine.

After I lay down on the table and a rectal ultrasound probe had been inserted, the area was locally anaesthetized and the first few gold markers were inserted into the prostate. After this, the gel was inserted (using some kind of syringe) between the prostate and the rectum, under ultrasound guidance.

The procedure wasn't very bothersome to me due to proper anesthesia. However, I was surprised when I got off the table and felt urine trickling down my legs. What had happened? As a result of having anesthesia, I had lost control over my sphincters and whenever I switched from lying down

to the upright position, my bladder emptied. A couple of diapers in my underwear relieved this problem and I walked to the train station. As I got out of my seat after a brief train ride I felt the urine flowing into the diaper. I made the doctors aware that future patients should be notified of this temporary inconvenience (only lasted a couple of hours).

I did have bowel complaints during radiation of the prostate and the lower abdomen (cramps, diarrhea, nausea). After making an adjustment to my diet (information I found on medical websites) the bowel complaints and the medications I needed (Imodium and Primperan) decreased significantly. The last complaints disappeared within a week after completion of the radiation to my stomach and the subsequent boost to the prostate.

I had no stomach complaints whatsoever anymore; although the prostate had been heavily hit during the last weeks and theoretically speaking, the rectum could have been affected as well. I am extremely satisfied about this technique and am recommending it to others. My hope is that other patients will have a similar experience and if they do, that this treatment may become the standard for prostate radiation.

Harm Kuipers ■