Interstitial brachytherapy for bladder cancer with the aid of laparoscopy

A.M. Nap-van Klinken[1], S.J.E.A. Bus[1], T.G. Janssen[1], M.P.R. Van Gellekom[1], G. Smits[2], E.M. Van der Steen-Banasik[1]

[1]Arnhems Radiotherapeutisch Instituut (ARTI), Arnhem, [2]Urology Department, Rijnstate Hospital, Arnhem

Since 2009, 40 patients with a T1/T2 bladder cancer have been treated at ARTI with interstitial brachytherapy via laparoscopy. Under general anesthesia, the tumor area is implanted under cystoscopic control with the aid of a laparoscope, and instruments are attached to the Da Vinci robot. Mapping is then done via a simulator photo and a CT scan. With this method, the patient has fewer complications and the average hospitalization time is halved, while a consistent quality of the implant is maintained. This method also shows a major reduction in the number of problems that can be attributed to the accessibility of the catheter.

Introduction

Patients with bladder cancer have been treated with interstitial brachytherapy at the Arnhems Radiotherapeutisch Instituut (ARTI) since 1973. Initially this treatment was carried out with radium needles followed by cesium needles. The Institute switched to implanting catheters in 1996. Until June 2009, catheters were implanted via an open procedure. At present, the catheters are placed via laparoscopy and, since September 2010, with the aid of the Da Vinci robot. This has advantages in many areas.

Annemieke Nap - van Klinken and Saskia Bus

Context

In the Netherlands, approximately 5,200 people are diagnosed with bladder cancer every year. The standard treatment of invasive bladder tumors is cystectomy. For patients with a solitary T1G3-T2 urothelial cancer <5 cm, treatment to save the bladder by using brachytherapy combined with external radiation is considered. Earlier studies show that brachytherapy results in a local control of between 70% and 88%. The five-year survival rate varies between 48% and 73%[1,2,6]. Approximately 90% of patients cured by radiotherapy retain an effectively functioning bladder[4,8].

Between 1996 and 1998, patients with bladder cancer were radiated at ARTI with a manual afterloading method using a low dose rate (LDR) iridium wire. Since the introduction of the pulse dose rate (PDR) afterloader in 1998, 77 patients at ARTI have been irradiated with the aid of interstitial brachytherapy. Forty patients have been treated via laparoscopy, 32 of whom were treated with the aid of the Da Vinci robot. Patients with stage T2 cancer received 20 fractions of 2 Gy externally, followed by a brachytherapy boost of 25 Gy in 10 pulses (33 patients via laparoscopy) or 28 Gy in 28 pulses (26 patients via an open procedure and 6 patients via laparoscopy). All regimens were administered within office hours only.

Twelve patients followed a different radiation regimen.

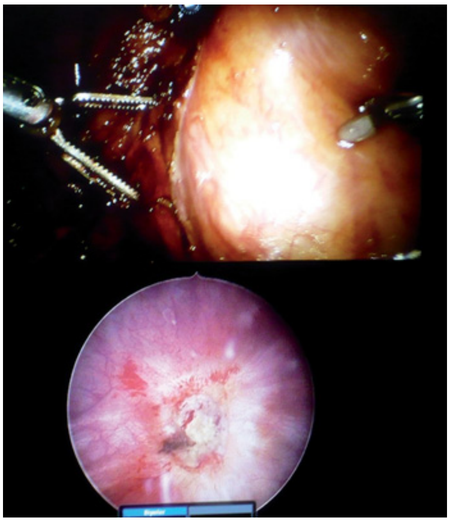


Figure 1: The illustration at the bottom shows the tumor area in the bladder via cystoscopy. In the illustration at the top, the cystoscope light is visible in the abdominal cavity via the laparoscope.

Implantation of the catheters

The use of laparoscopy for implanting the catheters has made the operation less invasive. The patient is given a general anesthetic and is placed in the Trendelenburg position. The laparoscope and instruments are inserted into the abdominal cavity through small incisions in the skin, and subsequently connected to the Da Vinci robot. The tumor area in the bladder is mapped with the aid of a cystoscope. The light of the cystoscope is visible in the abdominal cavity via the laparoscope (Figure 1). This is the area where the catheters are implanted. In some situations, a partial cystectomy is performed before the catheters are implanted.

The catheters can be implanted once the surrounding structures have been moved away from the implantation area. The radiotherapist inserts the needle with the catheter attached to it through the patient's skin, after which it is handled by the robot, which is operated by the urologist. With the robot the catheter is guided further into the abdominal cavity and through the bladder wall under cystoscopic control. The needle with catheter is then pushed towards the outside through the skin on the other side of the abdomen. The needle is then removed from the catheter.
All the catheters are placed in this way (Figure 2). Clips are placed on both sides of the Clinical Target Volume (CTV). These are visible on the CT scan and the X-rays. The catheters are fixed on both sides of the abdomen with buttons (Figure 3). The incisions in the skin are then sutured and the patient is transferred to the recovery room.

The catheters are prepared during the laparoscopy. The inner catheter is pushed down as far as possible; this stiffens the catheter and protects it against kinking. 0.5 cm of the catheter is cut off. A slightly curved 4.5 cm needle (Nucletron/Elekta), specifically developed for this procedure, is attached to the catheter. Small ridges on the needle ensure that it is firmly fixed in the catheter. The needles are only used once because, during implantation, the area where the needle is connected to the catheter is tightly squeezed, which means that the needle may become detached from the catheter during the next implantation.

Mapping/planning

Mapping for the purpose of the radiation plan is done using an anterior-posterior X-ray and a CT scan. The catheter is shortened on the simulator on the basis of the X-ray from the open side (the side where the needle was attached). To determine the length of the catheter, a thin metal wire of fixed length is introduced into the catheter. The end of the metal wire indicates the first source position. This must be located just past all the clips. This is repeated for all the catheters. An X-ray is made to get an overview of the catheters (Figure 4).
Also, a CT scan is made with the metal wires inserted in the catheters. The slice thickness used is 1 mm. The CT slices are imported into the Flexiplan (Nucletron/Elekta) planning program. The catheters are reconstructed on the CT slices. A step size of 2 mm between the source positions is selected. The active dwell positions lie between the clips that are left behind during the implantation. The dose points are located 5 mm from the catheters. The dwell times are calculated by dosing to an average of all the dosing points. Sometimes, improvements are made manually, but increasing dwell times should be done with caution in order to avoid too high a dose around the catheters (Figure 5).
The first pulse is often given on the day that the catheters are implanted. After the last pulse, the catheters are removed from the patient (Figures 6 and 7).

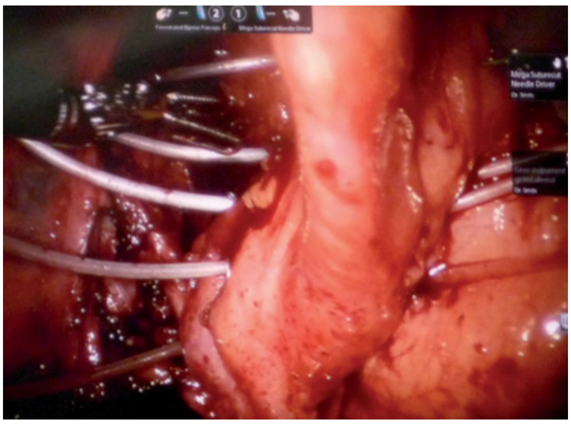


Figure 2: Laparoscopy image of 5 catheters implanted in the bladder wall parallel to each other.

Figure 3: Photo of the buttons that secure the catheters.

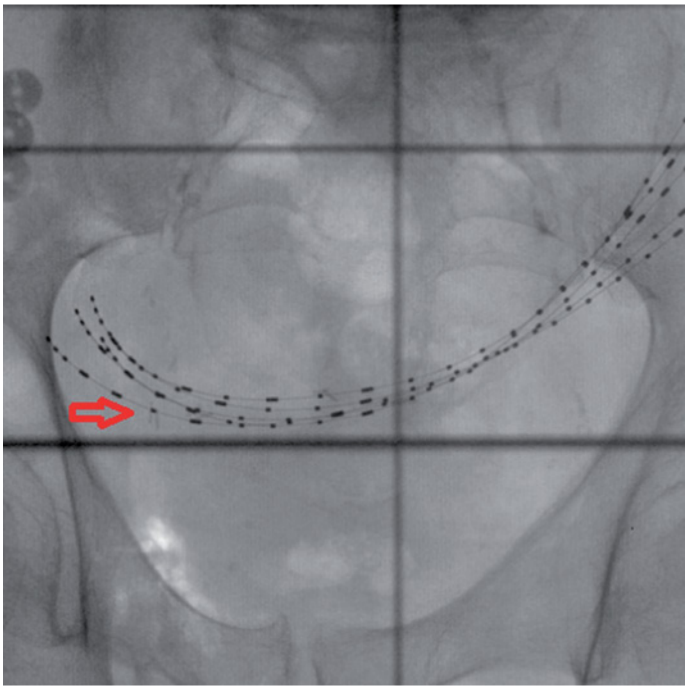


Figure 4: AP X-ray photo of a patient where 5 catheters are implanted in the bladder wall. The catheters are visible because of the metal wires. The clips are also visible in the photo. 2 of the 8 clips can be seen near the arrow.

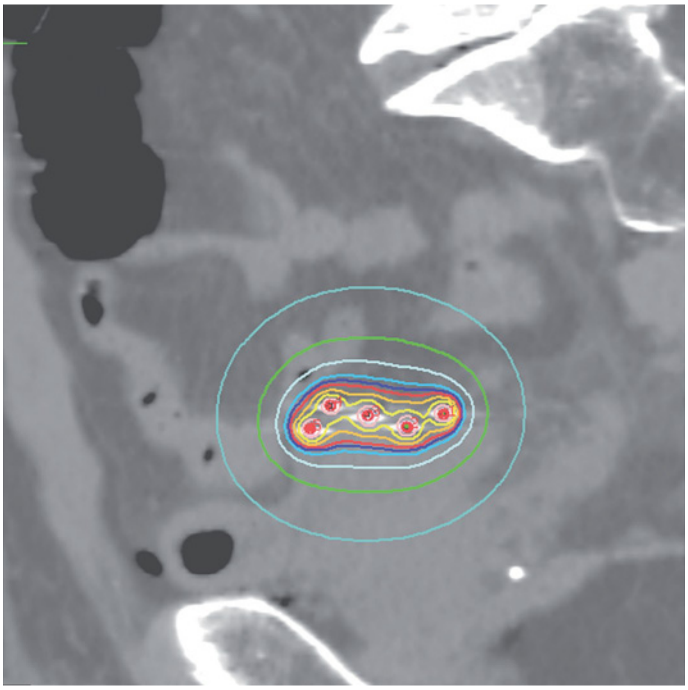


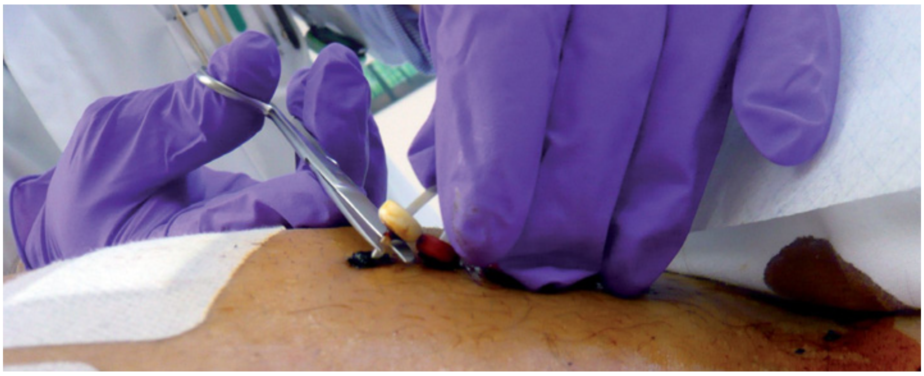
Figure 5: A sagittal cross-section of a patient where 5 catheters are implanted in the bladder wall. This mapping shows the dose distribution. The red line is the 100% iso-dose line.

Acute and late complications

Compared with an open procedure, implantation via laparoscopy has both physical and logistic advantages for the patient. The operation, as performed at present, is minimally invasive, resulting in practically no blood loss and a shorter operating time.

The reduction in hospitalization time, from an average of 16 days (6-90 days) to an average of 6.5 days (4-18 days) is particularly striking. Wound healing after an open procedure takes longer; one of the patients developed a serious bladder defect, which led to 90 days' hospitalization. 1 patient developed aspiration pneumonia and 1 patient had urine leakage after the partial cystectomy of a recurrent urachal tumor. After a period with an indwelling catheter, the defect underwent secondary closure.

Up to now, late complications have consisted of asymptomatic ulcers and one abscess of the TUR cavity in one patient, one year after TURB for in situ carcinoma. This patient was treated with antibiotics and hyperbaric oxygen.



Figures 6 and 7: The catheter is cut under the button and then pulled out of the abdomen on the other side.

Quality of the implant

One important aspect that contributes to the success of interstitial brachytherapy of the bladder is the quality of the implant. The catheters have to lie in parallel and with approximately 1 cm distance to each other in order to achieve a dose distribution that is as homogeneous as possible[7]. The quality of the implant is assessed on the basis of the following implant-specific parameters: Homogeneity Index (HI) and Overdose Index (OI). Since the CTV and the Organs At Risk (OAR) were not entered, the target-specific parameters could not be assessed. The HI indicates the size of the part of the target volume that receives 100% to 150% of the prescribed dose (Formula 1)[3,5].

The OI indicates the size of the part of the target volume that receives more than 200% of the prescribed dose (Formula 2)[3].

Formula 1: HI = (V100 – V150) / V100 * 100%
Formula 2: OI = V200 / V100 * 100%

10 patients were chosen at random from both group 1, who were patients implanted via an open procedure, and group 2, who were patients implanted via laparoscopy. The total active length of the catheters was comparable in both groups. The average total active length of group 1 was 14.75 cm and of group 2, 13.87 cm. HI and OI values of both groups are given in Figures 8 and 9. The average HI and OI values of group 1 were 57.3% and 19.8% respectively. The average HI and OI values of group 2 were 57.0% and 21.3% respectively.
An unpaired t test ($\alpha < 0.05$) showed whether the parameters of both groups differed significantly.
The p values found were: 0.16 and 0.85 for HI and OI, respectively. Since these were bigger than the significance level, no significant difference was shown in the quality of the implants. A trend over time was found in group 2: the homogeneity of the dose distribution increases, whereas overdosing decreases.

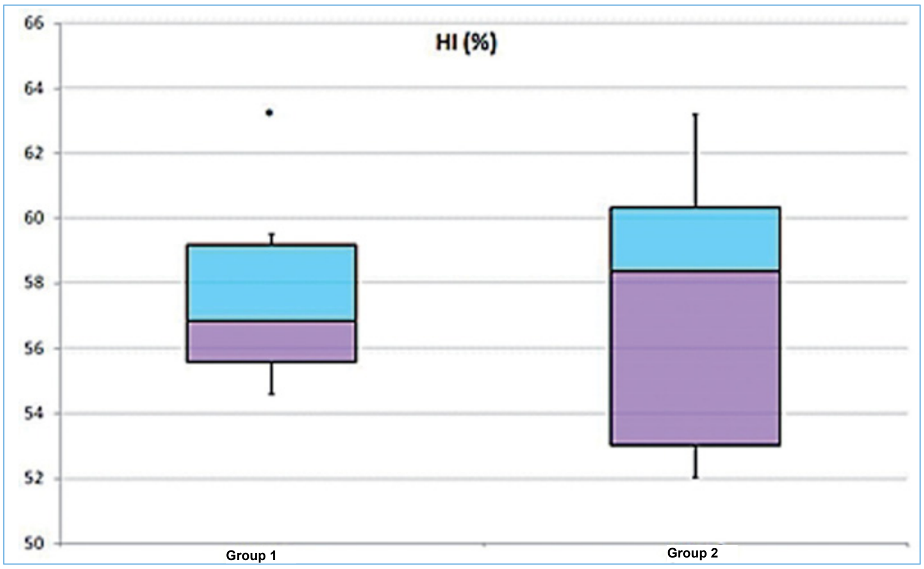


Figure 8: The HI values are indicated in a box plot for both groups. The box contains 50% of the data (25% percentile up to 75% percentile). The median is indicated by the horizontal line in the box. The error bars indicate the minimum and maximum values. If a data point deviates from the box length more than once, it is an extreme point, indicated by a *. 1 extreme point occurs in group 1 only.

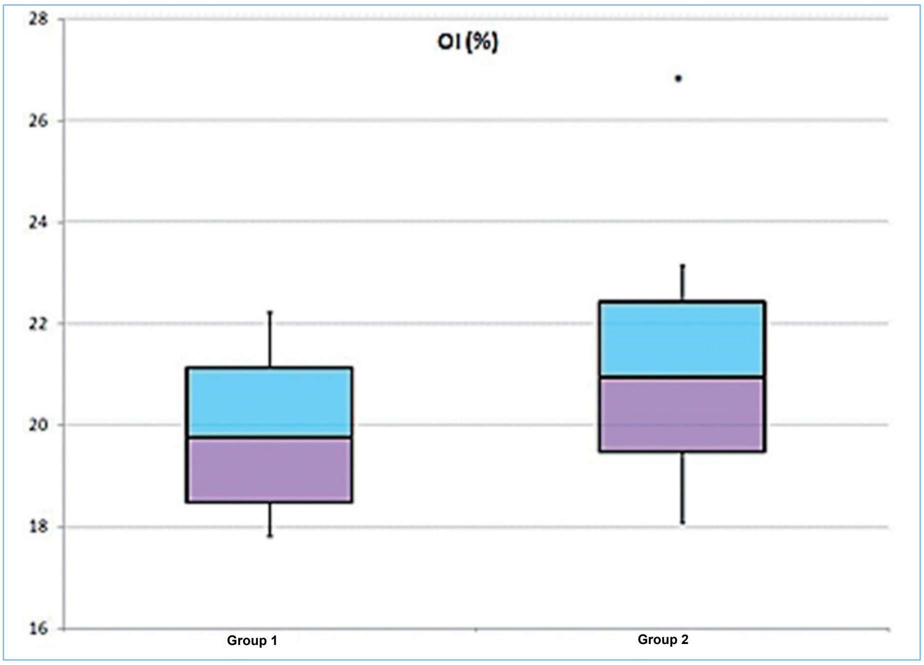


Figure 9: The OI values are indicated in a box plot for both groups. The box contains 50% of the data (25% percentile to 75% percentile). The median is indicated by the horizontal line in the box. The error bars indicate the minimum and maximum values. If a data point deviates from the box length more than once, it is an extreme point, indicated by a *. 1 extreme point occurs in group 2 only.

Discussion

Since 2009, implantation has been done using a laparoscopic method. In view of the short length of time and the relatively small number of patients, no conclusions can be drawn about the clinical results in the long term.
One noticeable result of implantation via laparoscopy is the significant reduction in problems during radiation. In 16 out of 26 patients who had an open procedure, we identified problems with 1 to 6 pulses, which were related to the accessibility of the catheter. Such problems can have consequences for the treatment. If a catheter was no longer accessible for the Ir-192 source, the plan had to be adjusted. In the new plan, the catheter, or part of it, is then no longer used. This does not mean by definition that the plan becomes worse. Often, by optimizing again, a clinically acceptable radiation plan can still be achieved. For this reason, a new plan was made for 2 of the 26 patients who had received 28 pulses. Since we started using the laparoscopic method, no further problems have occurred that are connected with the accessibility of the catheter. The reduction in problems since implantation via laparoscopy can be explained by a combination of different factors. The radiation regimen for the treatment is adjusted from 28 pulses to 10 because of the logistic burden for the nursing department.

In the case of 10 pulses, the inner catheter was reinserted in the catheter after each pulse, whereas in the case of 28 pulses, the patient remained connected to the afterloader. This increased the risk of deformation of the catheters due to reduced rigidity. Also, when implanting via an open procedure, spacers were used, which were placed in the bladder in order to achieve an equal distance between the catheters. The spacer appeared to have an important influence on the deformation of the catheter. This could cause an obstruction for the Ir-192 source. The use of spacers guaranteed the quality of the implant. Since we started using the laparoscopic method, the use of spacers has been omitted. In fact, it is no longer possible to remove the spacers in an easy way after radiation. Therefore, the analysis of the quality of the implant is an important part of the evaluation of implantation via laparoscopy. It is not necessary to use a Da Vinci robot for implantation of the catheters. However, the robot does make the implanting of the catheters easier, because movements can be made with greater precision.

Developments

In addition to implantation via laparoscopy, we are looking with Nucletron/Elekta for possible improvements to the existing catheter. A new catheter is being developed at the moment to which a needle is already attached. The catheter will be supplied pre-assembled as a disposable and is ready for immediate use. The catheters can then be supplied with needles of different lengths and with several curves. In addition, the catheter will have a centimeter marking so that during the laparoscopy, the range of the target area can be assessed.

At the moment, we are investigating whether the patient's bladder fill influences the quality of the implant. During implantation, the patient's bladder has been approximately filled with 150 cc. The CT scan and radiation take place with an empty bladder. At present, a second CT scan is made, with the bladder being filled with 150 cc NaCl via the bladder catheter. We are investigating whether this gives an improvement in the configuration of the catheters and the associated dose distribution.

Conclusion

Bladder implantation via laparoscopy seems to be an effective technique where the quality of the implant remains guaranteed. The hospitalization of the patient is halved. The implanting of the catheter is minimally invasive and the acute complication rate is low. This method also results in a major reduction in the number of problems that can be attributed to the accessibility of the catheter. Of course, good multi-disciplinary cooperation is required between urologists, radiotherapists and support personnel in order to achieve optimal treatment.

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