

Irradiation techniques • Technika napromieniania

A new method of targeted intraoperative radiotherapy using the orthovoltage photon radiosurgery system

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The aim of this study is to present a new method of intraoperative radiotherapy (IORT) using the PRS400 Photon Radiosurgery System. IORT is a method of irradiation inside the tumor bed or tumor, aimed at dose escalation and local control probability increase and sparing normal tissues. IORT can be used alone, or in combination with external beam radiation therapy. The PRS400 Photon Radiosurgery System is a mobile miniature X-ray source dedicated for IORT. PRS400 generates soft X-ray with a maximum emitted energy of 50 keV. The depth dose falls very rapidly with depth of the soft tissue ($1/r^3$). PRS400 can be used in different anatomical localisations. The advantage of PRS400 is that it can be used in any operating room, usually without special shielding.

Nowa metoda śródoperacyjnej radioterapii przy użyciu rentgenowskiego aparatu do radiochirurgii

Celem pracy jest przedstawienie nowej metody radioterapii śródoperacyjnej (RŚ) przy wykorzystaniu urządzenia PRS400. RŚ jest metodą leczenia pozwalającą na podwyższenie dawki w guzie lub w obszarze łoża po guzie, w celu zwiększenia prawdopodobieństwa miejscowego wyleczenia nowotworu, przy równoczesnym oszczędzeniu zdrowych tkanek. Najistotniejszą częścią PRS400 jest miniaturowe źródło promieniowania rentgenowskiego, wytwarzające miękkie promieniowanie X o maksymalnej energii 50 keV. Spadek procentowej dawki głębokościowej jest bardzo szybki ($1/r^3$). Zestaw PRS 400 może być zastosowany w leczeniu nowotworów w różnych lokalizacjach anatomicznych. Zaletą PRS400 jest możliwość wykonania RŚ w każdej sali operacyjnej bez zastosowania specjalnych osłon.

Key words: radiation therapy, intraoperative radiotherapy

Słowa kluczowe: radioterapia, radioterapia śródoperacyjna

Introduction

Over the last years we have observed a renaissance of intraoperative radiotherapy (IORT). IORT is based on the delivery of a large single dose of electrons (IOEBRT) or X-rays (IOXRT) through a surgical wound to irradiate the tumor or the tumor bed. High dose rate afterloading brachytherapy (IOHDR) can also be used as a form of intraoperative treatment. IORT can be used in the treatment of different cancer locations: head and neck, breast, brain, stomach, pancreas, extrahepatic bile ducts, colorectum, lung, bladder, cervix, uterus, vagina and soft

tissues [1-3]. A single dose of IORT is more effective than an identical dose of conventional fractionated external beam radiation therapy (EBRT). Tumor control probability increases with the escalation of the radiation dose. IORT allows to protect normal tissues, which may be shielded or placed outside of the irradiated volume. Initially, IORT was used as a sole treatment modality; doses ranged from 25 Gy to 40 Gy [4]. More recently, IORT has been used in combination with EBRT [5]. In a majority of cases a 10-20 Gy boost dose was used. Application of EBRT should be started 2-4 weeks after surgery.

Description of the PRS400 Photon Radiosurgery System

The PRS400 Photon Radiosurgery System (Carl Zeiss Surgical GmbH) is a portable equipment designed for intraoperative radiotherapy [6, 7]. The PRS400 has been approved by the FDA for intraoperative treatment. This

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Figure 1. The PRS400 Photon Radiosurgery System consists of the X-Ray source and the control console

system is also called the INTRABEAM™ System, and can be used in any operating room, usually without special shielding. There are no logistic and technical problems with patient transportation from the operating room to the radiotherapy department and back. This system can be used to irradiate the tumor bed, as well as the tumor itself. For intracranial applications the PRS400 is combined with a stereotactic frame (the ACCUBEAM™ System) [8, 9]. The PRS400 Photon Radiosurgery System consists of the X-Ray Source (XRS) and the control console (CC), (Figure 1). The XRS is placed in a special mobile arm, keeping the applicator stable in the desired position during the IORT. XRS is small (17.5 cm x 11 cm x 7 cm) and it weighs only 1.62 kg. The XRS is equipped with a 10 cm long probe (3.2 mm diameter). This probe is enclosed in a spherical applicator, which is placed in the tumor bed. The XRS is connected to a control console with a low voltage cable (max. 15V) and plugged into 2-phase 220 V power. There is no risk of an electrical hazard to the patient and the surgeon. The CC is used to set up treatment parameters and control the XRS during operation.

Three values of high voltage are generated within the XRS: 30, 40 or 50 kV. The currently used intensities are 5, 10, 20 or 40 μ A. X-rays are generated by an electron beam which strikes the tip of the probe. For 50 kV voltage the maximum emitted X-ray energy is 50 keV, but the effective energy is approx. 20 keV. The dose rate is related to the diameter of the applicator and the distance to the applicator and ranges from 0.28 Gy/minute for 5 cm to 13 Gy/minute for 1 cm. The radiation surface is near to spheric. In soft tissue the delivered dose decreases very rapidly ($1/r^3$), due to the low energy of the X-ray. In the distance of three meters from the radiation source, the dose rate is lower than 20 μ Gy/min.

Before each IORT verification tests of the system, calibration procedures and treatment time calculations are performed by medical physicists. The verification procedures are relatively time-consuming (about 2-3 hours). For this reason the PRS400 system is usually

prepared on the day before the application. The manufacturing company recommends periodical calibration of the XRS to quantify the depth-dose rate characteristics. The XRS is not sterile, during surgery it is covered with a sterile transparent plastic bag. The applicators are sterilized before each treatment session.

The procedure of IORT

IORT is an interdisciplinary procedure, which requires good cooperation of the members of the treatment team, i.e. radiation oncologists, surgeons, anesthesiologists, nurses, radiation therapists and physicists. After surgical resection, the radiation oncologist and the surgeon determine the volume for irradiation. The choice of the applicator size depends on the tumor or the tumor bed. The diameters of spherical applicators range from 1.5 to 5.0 cm with an 0.5 cm step (Figure 2). The sterile applicator is inserted into the tumor bed (Figure 3). The normal tissues are shielded, if necessary. Shields can attenuate radiation approximately ten times (equivalent of 0.05 mm Pb screen for energy of 50 keV). The control console is located outside the operating room. The radiation therapist selects energy, dose rate and delivered dose. At any time, the operator of the CC may interrupt the IORT. The treatment time depends on the applicators size and the selected dose. The whole procedure of IORT is completed in approximately 20 to 40 minutes. During



Figure 2. The set of spherical applicators



Figure 3. The applicator immobilization inside the tumor bed

radiotherapy, the anesthesia monitoring system is located outside of the operating room, thus allowing to supervise the patient. A movable shield is placed in the entrance to the operating room, allowing the anesthesiologist to observe the patient directly.

Discussion

Local tumor control (LTC) is the most important issue in oncological treatment. The probability of TLC increases with higher doses. The planned dose often cannot be delivered by external radiotherapy because of normal tissue reactions. IORT is one of the methods of dose escalation. Thus, the therapeutic gain of the IORT is achieved by the dose increase within the tumor or within tumor bed and spares normal tissues. In this type of radiotherapy, the radiation injury of normal tissues could be minimized by shifting from the irradiated field, shielding or excluding normal tissue by using appropriate electron beam energy.

The most common sequelae of IORT are peripheral nerve, bile duct and ureter injuries. In patients with locally advanced colorectal cancer the probability of causing neuropathy increases with doses exceeding 15 Gy [10]. The obstruction of ureters and bile ducts can cause renal and liver dysfunction. The pancreatic duct is particularly sensitive. Vascular injury can be observed with doses exceeding 30 Gy [11]. Other complications have seldom been reported. The ratio of postoperative complications remained the same, irrespectively of whether IORT or surgery only was applied.

Direct visualisation of the tumor during surgery allows for greater accuracy in determining treatment volume. IORT limits the likelihood of missing surgical margins, the risk of geographical error and marginal recurrence. This method of radiotherapy minimizes the risk of sad misses, thus being contrary to brachytherapy [12].

In many cancer locations, IORT is used as a sole adjuvant treatment modality. In the treatment of gastric cancer IORT is performed directly after tumor resection and before oesophagoenterostomy. Abe irradiated the tumor bed and the regional lymph nodes using a single dose, which ranged from 18 Gy to 40 Gy [1, 2]. Nodal metastases were controlled by a single dose higher than 30 Gy. IORT was also used in palliative treatment of inoperable tumors.

It appears, that a combination of IORT and EBRT may allow for better local tumor control and should improve the results of treatment. The tumor or the tumor bed with regional lymph nodes are irradiated from fractionated EBRT. The IORT boost is delivered to regions at a high risk of recurrence. Application of IORT can shorten the treatment time by, approximately, 1-2 weeks. In the radical treatment of abdominal malignancies sole EBRT is insufficient. Unlike in IORT, dose escalation from external beam radiotherapy can cause dangerous radiation injury. EBRT can be used both as preoperative and postoperative treatment. Radiotherapy

should be conventionally fractionated up to the total dose of 45-50 Gy. Preoperative EBRT would allow to decrease the tumor volume and should facilitate the operation. Consequently, the volume of boost is decreased.

The application of IORT using the PRS400 system has been investigated. The number of published clinical studies is too limited to recognize IOXRT as standard treatment [6, 7]. Intraoperative electron-beam radiation therapy (IOEBRT), intraoperative high dose rate brachytherapy (IOHDR) and intraoperative X-rays radiation therapy (IOXRT) are all different techniques of intraoperative radiotherapy. From the radiobiological point of view, it is not possible to transfer IOEBRT or IOHDR experiences directly to IOXRT. IOEBRT allows for a more homogeneous dose distribution within target than X-rays. The accelerators can produce electron beams of different energies from 6 MeV to 25 MeV. The surface dose (Ds) of electron beams ranges from 75% for 6 MeV to almost 100% for 18 MeV [13]. Ds is proportional to energy of electrons. For lower electron beam energy build up dose region may play have clinical impact. The dose delivery to CTV may be approximately 20% lower, than the calculated dose. Reni observed the influence of electron beam energy on local control [14]. Local control of pancreatic cancer was 17% for 6 MeV compared to 37% for higher beam energies. It is clinically significant that the percentage of the depth dose depends on the field size. There is a more rapid dose fall-down for smaller fields. The advantage of electron beams is the big dose gradient which allows to protect critical organs. Usually 80% or 90% isodoses are used for delivered dose calculations. For IOHDR the dose inhomogeneity is smaller than for IOXRT. IOXRT and IOHDR achieve the maximum dose on the surface of applicator. The percentage depth dose from IOXRT is related to applicator size, which results in greater heterogeneity of dose within the target volume and decreases faster for smaller applicators. This dose distribution is advantageous for normal tissues, but not for the target volume. We recommend a standard depth to a dose calculation of 5 mm or 10 mm. It is necessary to report a contact dose.

A limitation of IORT is the accessibility of the site limited by the shape of the applicator. IOEBRT sometimes may be difficult to use in selected site, e.g. the head and neck, the brain, the anterior abdominal wall, the subdiaphragmatic areas, the anterior and lateral pelvic walls, due to the size and build of the applicators. At The Ohio State University, IOHDR was used in such cases [15]. The PRS400 can be easily used for such locations because the diameter of the smallest applicator is 1.5 cm. However, the disadvantage of PRS400 is the fact that only spherical applicators are used.

Conclusions

The main advantage of IORT is the very accurate localisation of the target volume. It allows to escalate the dose to the tumor or the tumor bed, and thus the probability of the locoregional control may increase.

Surrounding normal tissues are spared and radiation injuries are rare.

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