

Extending indication for Radiofrequency Ablation (RFA) in cancer surgery

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Rezumat

Lărgirea indicațiilor Ablației prin Radiofrecvență (RFA) în chirurgia oncologică

Ablația prin radiofrecvență (RFA) reprezintă una dintre metodele de succes pentru ablația termică a tumorilor nereze-cabile. Efectul tumoricid al acestei metode constă în conversia în țesuturi a energiei electromagnetice în energie termică. Termenul se referă la curentul electric a cărui frecvență atinge valori înalte, în medie 480 KHz. Metoda presupune inserția în determinările tumorale parenchimotoase de ace bipolare. Afectarea termică tisulară depinde deopotrivă de temperatura atinsă și durata. Cea mai frecventă utilizare este în tumorile hepatice (metastaze, hepatom) nereze-cabile sau cu contra-indicație de chirurgie, vizibile ecografic. Noi am extins indi-cațiile și spre alte localizări tumorale: tumori de col uterin (stadiile II, III, IV) însoțite de metroragii, RFA fiind folosită în scop hemostatic și de reducere a volumului tumoral, tumori genitale, blocuri adenopatiche latero-aortice în scopul reducerii masei tumorale, metastaze (muschi psoas, os sacru), sarcoame retroperitoneale, cu rol hemostatic și de reducere a volumului tumoral. Lucrarea își propune prezentarea unei note preliminare bazată pe 24 cazuri. Rezultatele au demonstrat utilitatea aplicării RFA în scopul reducerii masei tumorale și rolul hemostatic al metodei. Nu s-au înregistrat complicații.

Cuvinte cheie: ablația prin radiofrecvență, hemostază, tumoră de col uterin, tumori pelvine

Abstract

Radiofrequency ablation (RFA) represents one of the successful methods for the thermal ablation of unresectable tumors. The tumoricidal effect of this method consists in the tissular conversion of electromagnetic energy into thermal energy. The term refers to the electric current, whose frequencies reach high values, 480 KHz on average. The method involves the insertion of bipolar needles in parenchymal tumors. The thermal tissue damage depends on both the temperature reached and the duration. The most frequent use is for unresectable hepatic tumors (metastases, hepatoma) or for those with a contraindication for surgery, visible on ultra-sound. We have also widened the indications to other tumoral locations: cervical cancer (stages II, III, IV) accompanied by metrorrhagia, RFA being used hemostatically and with the purpose of reducing the size of the tumor, genital tumors, lateral-aortic lymph blocks to reduce the tumoral mass, metas-tases (the psoas muscle, the sacrum), retroperitoneal sarcoma, with a hemostatic role and also to reduce the size of the tumor. The paper aims to present a preliminary situation based on 24 cases. The results have shown the usefulness of the application of RFA with the purpose of reducing the tumoral mass and the hemostatic role of the method. No complications were recorded.

Key words: radiofrequency ablation, hemostasis, cervical tumor, pelvic tumors

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Introduction

The oldest story about cancer can be found in the Egyptian papyrus discovered in the 19th century by Edwin Smith and Ebers which contained the first "medical record", dating from 2,500 B.C. and describing 8 cases of breast tumors cancer treated by cauterization. (1,2). Hippocrates stated that: "What cannot be healed with the scalpel should be treated with fire, and what cannot be healed with fire should be considered incurable"(3). Later on, in the 19th century, the Frenchman Henri Becquerel turned electricity into heat, thus founding electrocauterization (4). In 1891, Jacques-Arsene d'Arsonoval used alternating electric current with a frequency of 20 kHz or even higher, producing heat in the tissue, without causing neuromuscular excitation (5). In 1928, two Americans, Harvey Cushing and William Bovie T, devised a generator of alternating electric current which worked within the radio-frequency range and a small electrode (cautery) which could be used to cut and/or stop bleeding in the tissues (6). Radiofrequency ablation (RFA) was introduced in Italy in 1980 for the treatment of hepatic tumors. In 1995 Rossi reported the first clinical studies, using RFA for hepatic tumors smaller than 3 cm (7). In the USA, in 1996, Kenneth Tanabe and Naum Goldberg performed the first RFA in a patient with a liver tumor, and in 1997 Curley used it for unresectable hepatic tumors and metastases. (8)

The term radiofrequency (RF) refers to the electric current whose frequency reaches values between 200 and 1.200 KHz (480 KHz on the average at a power of 200 W). The electric current produced around the electrode causes ionic agitation in the tissues and the molecular friction generates heat, which can be controlled by modulating the dissipated energy. The evaporation of intracellular water and clotting necrosis (the irreversible coagulation of proteins, enzymes, intranuclear proteins and DNA) depend on the temperature reached and on the duration of the application of the electromagnetic energy. Cellular death occurs at 42°C, but it may take at least 60 minutes, depending on the tissue involved. Irreversible cellular damage occurs between 46-60°C, depending of the duration of the exposure (cellular death occurs in 4-6 minutes at 50-52°C). The almost instantaneous distortion of proteins occurs between 60-100°C. The objective is to heat the tissues at 50-100°C for 4-6 minutes without causing charring. Temperatures of 105°C cause boiling (microbubbles of nitrogen released from the cells) and charring, followed by the sudden growth of tissular impedance and limited spread of heat and clotting necrosis, thus preventing ablation. (9)

Material and Method

The method involves the insertion of probes (bipolar needles) in the tumors, under image guidance (ultrasound, CT scan, laparoscopy). For liver tumors, the morbidity of the procedure is below 20%, and mortality ranges between 0-2% (10). The applicators are connected to the radiofrequency generator and the cooling pump of the electrode. The model of device used (CelonLab Power) performs tumor ablation in an bipolar or

multipolar manner, according to the number of electrodes inserted into the tumoral mass, thus increasing the ablation area up to a diameter of 4-7 cm. The electrode used (14-18 g) has internal cooling -cool-tip- (CelonproSurge) through a continuous flow of saline and provides a low impedance by delivering the maximum quantity of energy into the highest possible ablation volume, simultaneously avoiding charring. Probes under the shape of a cylinder or a sphere/ovoid (1-3 needles are used) help to achieve tumoral destruction. The tissular injury = (the energy applied x tissue resistance) – lost energy. The use of needles for the tumors located near the blood vessels with a diameter larger than 3 mm does not cause lesions to the vascular wall due to the blood flow which dissipates the heat (heat sink) (11). Tumors of 3-5 cm can be destroyed in a single application. The dead cells are absorbed by the immune system in 3-4 weeks. (12). The most frequent use is in liver tumors (metastases, hepatocellular carcinoma) (13). RFA is also used for other tumoral locations: kidney, lungs, bone, breast, thyroid, prostate, adrenal gland, brain tumor, and sarcoma. (14, 15, 16)

We have widened the indications of RF. The paper aims to present a preliminary situation based on 27 applications (24 patients, 3 of which underwent a double application of RF). The results demonstrated the usefulness of RF application to reduce the tumoral mass and the hemostatic role of the method. Contraindications: infected tumors, visible and uncontrollable changes in the coagulation test, thrombolytic count < 50,000, pregnancy or breastfeeding. The patients gave their written consent for the procedure, and the biopsy of the tumor was mandatory. An interdisciplinary examination was performed (surgery, oncology, radiotherapy).

Cervical neoplasms, stage II, III and IV (FIG.O) 14 cases accompanied by vaginal bleeding and severe secondary anemia in female patients aged 43-74 (the average age was 55). The histo-pathological results showed: 13 cases of squamous cell carcinoma (epidermoid) and one case of endocervical adenocarcinoma. The exploration performed prior to the ablation included: laboratory tests (blood count, liver enzymes, serum bilirubin, blood glucose, serum urea, creatinine, coagulation tests, blood group, tumor marker CA-125), imaging examinations (abdominal/vaginal ultrasonography, chest, abdominal and pelvic CT/MRI) and tumor biopsy. The anesthesia was general with orotracheal intubation or spinal, and the patients were administered antibiotics (3rd and 4th generation cephalosporin and metronidazole injections) at the time of the induction of anesthesia as well as 3-4 days after the ablation. The intervention was performed vaginally, by introducing three RF needles directly at the level of the cervical tumor, under intravaginal ultrasound control, at a power of 75W, using an average of 50kJ during 20 minutes. The evolution of the necrotic process was followed by the appearance of gas bubbles, and the ablation was performed from the deep to the superficial layer. (Fig. 1 and 2). The bleeding from the tumor stopped after the first session. The patients followed the radio/chemotherapeutic procedures (RT/PCT) (one of the patients refused the RT/PCT adjuvant treatment). The excision specimens from the cervical neck did not show any

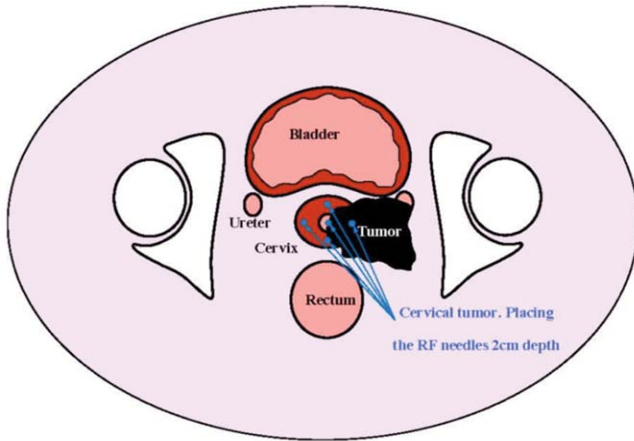


Figure 1. Stage IIIb cervical tumor with ureterohydronephrosis; positioning of RF needles

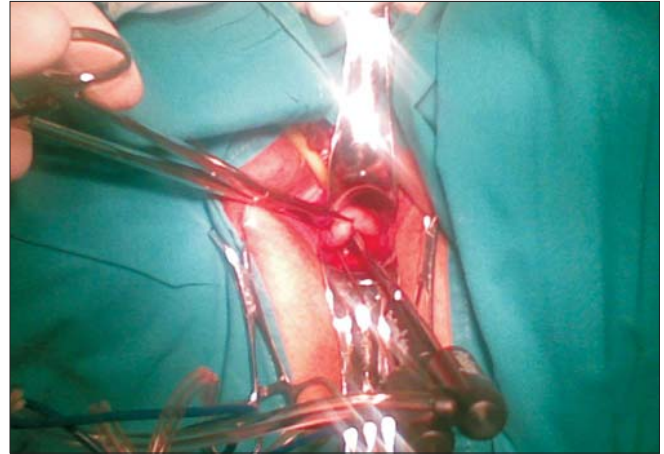


Figure 2. Cervical tumor. Placing the RF needles



Figure 3. Stage IIIb ovarian cancer with metastases in the interaorto-caval Lymph nodes, before RF



Figure 4. Stage IIIb ovarian cancer. RFA at the level of interaorto-caval Lymph nodes

areas of necrosis nor any residual tumor cells post radiotherapy (Wertheim operation – 4 cases).

Stage IIIb cervical neoplasm, post radiotherapy, no response to the treatment (2 female patients, 2 applications) with 4th degree ureterohydronephrosis, RF being used to reduce the size of the tumor and to release the ureters from the tumor mass (25W15Kj20 min). The CT scan after one year showed no tumor recurrence in the working area and a functional kidney.

Stage IIIc ovarian neoplasm (one patient, 2 applications). A total hysterectomy, a bilateral anexectomy and an omentectomy were performed, followed by polichemotherapy. Tumor relapse occurred in the primitive and promontorian iliac Lymph nodes. RFA was performed with the excision of the tumoral material. The following relapse occurred after a year in the interaorto-hollow lymph nodes for which RFA was performed, followed by the surgical excision. The CT scan one year later postoperatively showed no latero-aortic tumor recurrence at the level of the promontory as well. (Fig. 3, 4, 5). Other applications of RF:



Figure 5. Stage III b ovarian cancer with metastases in the interaorto-caval Lymph nodes, after RF

metastasis of hepatocellular carcinoma with sacral localization (one female patient, one application), retroperitoneal sarcoma (2 patients, 2 applications), RF been used with a hemostatic role and to reduce the volume of the tumor. Cecum tumor with invasion of the psoas muscle (one patient, 2 applications). After the right hemicolectomy a bleeding tumoral area was left in the psoas muscle, RF being thus applied with a hemostatic role and to reduce the volume of the tumor. Postoperatively, the patient underwent chemotherapy. After one year, the CT scan showed the tumoral recurrence in the psoas muscle, and the CEA (the carcinoembryonic antigen) was double than normal. The surgical intervention was performed and a firm area was found at the level of the psoas muscle. The extemporaneous biopsy of the area revealed the metastasis of the adenocarcinoma. The tumoral formation in the healthy psoas muscle was excised (HP check) up to the periosteum, and the bleeding borders of the muscle were subjected to RF (75 W/10Kj/10min). The CT scan and CEA marker were normal after 24 months.

Presacral rectal tumor recurrence, after the rectal amputation (4 applications, 3 patients), RF being used with a hemostatic role and to reduce the volume of the tumor (50W/25 Kj/30min). After 6 months, the patients presented no tumor recurrence at the CT scan examination.

Results

The bleeding stopped after the first use of the procedure, irrespective of the histopathological type of the tumor, without having to repeat the application of the radiofrequency. The patients did not present post ablation complications (fever, leukocytosis, pain). Broad spectrum antibiotics were administered (3rd and 4th generation cephalosporin + metronidazole) during 3 - 4 days to prevent the infection of the area with coagulation necrosis. During the monitoring period of the female patients with cervical tumors (2 years) no occurrence of recto-bladder-vaginal fistulas was recorded, no abscesses and no recurrence of bleeding (in the case of the vaginal approach) were recorded and no urethral fistula (in the 2 cases of intraperitoneal approach for the ureterohydronephrosis). The female patients with cervical tumors who experienced vaginal bleedings were hospitalized for 3-4 days, while the rest of the patients in whose case Rf was performed were hospitalized for 7-10 days. None of the patients were treated on an outpatient basis.

The patients were monitored after a week, then after a month to find the possible infection of the necrosis areas, then every 3 months for 2 years, clinically, by examining the blood count, the tumor markers (CA-125, ACE) and by ultrasound (CT, MRI, PET-CT) (for tumor recurrence). In all the patients, both the ultrasound examination performed during the radio ablation process, and the check up examination performed after the procedure showed a reduction of the volume of the tumor and the absence of the recurrence in the working area. Only one patient with a tumor of the cecum invading the psoas muscle presented with tumor recurrence in the psoas muscle post RF, after one year, requiring the repetition of the

procedure and the surgical excision, but had a good evolution after 2 years. RF was used in both the first and the second application, with good results, at the level of the psoas muscle in the surgical excision area of the tumor, especially for the hemostasis and less for the destruction of the tumor.

The surgical excision was possible after 14 RF procedures (51.8%) and consisted in Wertheim operations (4 cases of R0 resection), tumor mass reduction (10 cases with R1-R2 resection). The rest of the patients had no indication for surgical involvement. All the patients underwent radio/chemotherapy after the performance of the radioablation, according to the indications of the specialists in oncology/radiotherapy.

Discussion

REFA is efficient (100%) for the cervical tumors accompanied by vaginal bleeding, leading to hemostasis 20 minutes. The use of the probe for intravaginal brachytherapy and the external irradiation had the same effect, i.e. hemostasis, within 24-48 hours for the female patients in stages IIb, III b or IVa FIGO, but only 85% of the female patients presented with pelvic recurrence after 24 months from the irradiation. (17). Our patients showed no tumor recurrence at the site where RF was performed and there were no complications from the pelvic irradiation (enteritis, rectitis or radix cystitis, asthenia, anorexia, nausea, pancytopenia, recto-bladder-vaginal fistulas). RF allows its repetition without any adverse effects. It is a possible solution (sometimes the only one) in the case of advanced neoplasms, irradiated with the maximum dose allowed, the alternative of which would be massage, intrapelvic arterial ligatures – Thoma Ionescu's quadruple ligature – the uterine/ hypogastric artery, the lombo-ovarian ligaments, the uterosacral ligaments, the round ligaments, and to which chemotherapy can be associated. RF was used palliatively in the advanced stages of the disease, sometimes after the failure of other palliative treatments, thus providing survival with a better quality of life and facilitating the chemo/radio therapeutic adjuvant treatment.

Radiofrequency ablation is recognized among the therapists, in comparison with the embolization of the uterine artery which is mainly used to achieve hemostasis, which reduces the vascularization at the level of the tumor, but the tumor cells are deprived of oxygen and multiply with more difficulty, thus becoming less sensitive to radiation. After the embolization the following may appear: pelvic pain, leukocytosis, fever, pelvic abscesses, bleeding, bladder-vaginal fistulas, sometimes the bilateral catheterization of the femoral artery being necessary and the repetition of the procedure (18, 19). We did not have these complications after radioablation. The localization of these tumors in the vicinity of the large vessels (the abdominal aorta, the inferior vena cava, the iliac vessels), of the dilated ureter (stage IV ureterohidronephrosis) did not constitute an obstacle for the use of RF, „heat theft” allowing the ablation of the tumors up to their vicinity (inter-orto-cava lymphadectomy, pelvic reduction tumorectomy). Research has shown that the administration of antiangiogenesis /antivasular agents would diminish the blood flow at the level

of the tumor, thus reducing the dissipation of the heat and favoring the action of RFA to reduce the volume of the tumor. Studies show that the high temperature generated by RF allows the activation of the cytostatic molecules within the tumor and the increase of the effectiveness of chemotherapy (doxorubicin), while the association of RFA with brachithery would be beneficial by adding the effects and could be used in the outpatient treatment of cancer (basically a 1-day cancer treatment), whereas in the case of small tumors, RFA could replace surgery in the future (20). Moreover, the U.S. National Cancer Institute recommends cryotherapy in the standard treatment of cervical neoplasms stage 0 (carcinoma *in situ*).

Conclusion

Radiofrequency:

- Achieves local hemostasis and the reduction of the volume of the tumor;
- Allows the bipolar current to limit its effect to the level of the tumoral area, thus reducing the effects upon the nearby anatomical structures;
- A number of 1-3 applicators may be used to widen the area of tumor destruction;
- Achieves an efficient coagulation which decreases the risk of relapse and the repetition of the treatment;
- Favors the association with radio and/or chemotherapy;
- In the future, we also plan to use RFA in the treatment of the benign tumors of the uterus (fibroids), accompanied or not by bleeding, and performed under transvaginal ultrasound control or percutaneous laparoscopy. The data from literature are favorable regarding the use of RF in benign uterine tumors. (21)

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