History of Image-Guided Tumor Ablation

1

Hester J. Scheffer

1.1 Cancer: A Brief History

The oldest descriptions of cancer can be found in ancient manuscripts. Fossilized bone tumors and the records of Egyptian mummies provide material evidence. The oldest known account of cancer dates from approximately 3,000–2,500 B.C. It is possibly attributable to Imhotep, an Egyptian physician and architect. The papyrus describes eight cases of tumors or ulcers of the breast, which ancient physicians treated by cauterization with a tool called the "fire drill." The papyrus continues the narrative by stating that "there is no effective treatment" [1].

Twelve centuries later, these tumors obtained their modern name – cancer. The word cancer is credited to the Greek physician Hippocrates (Kos, Greece, 460–370 B.C.). Considered the "father of medicine," Hippocrates employed the words 'carcinos' and 'carcinoma' in his descriptions of non-ulcer forming and ulcer forming tumors. Carcinos refers to the familiar zodiac sign Cancer, the Crab. The Greeks used this term because of the tendril-like projections. Hippocrates believed that both cancer and depression developed when the four "humors" or bodily fluids – black bile, yellow bile, phlegm, and blood – fell out of balance with one another, allowing black bile to collect in excess in whichever part of the body the cancer affected. From Hippocrates onward, the humoral theory was adopted by the prominent Greek physicist Claudius Galenus in the second-century A.D. and by Roman and Persian physicians. This theory' dominated and influenced Western medical science for the next 1300 years [2].

H.J. Scheffer
Department of Radiology and Nuclear Medicine, VU University Medical Center,
De Boelelaan 1117, 1081 HV Amsterdam, Netherlands
e-mail: hj.scheffer@vumc.nl

M.R. Meijerink et al. (eds.), *Irreversible Electroporation in Clinical Practice*,
https://doi.org/10.1007/978-3-319-55113-5_1

The next great wave in cancer scholarship and understanding came with the Renaissance, when scholars began to refine their understanding of the human body. Following the development of the modern scientific method in the Renaissance, scientists began to apply this to the study of disease. The Belgium physician and anatomist Andreas Vesalius (1514–1564), considered the founder of modern human anatomy, used autopsies to identify and understand anatomic structures that had previously been a mystery. No matter how hard Vesalius sought to confirm Hippocrates's theory of black bile, he failed to find this sinister porter of cancer and depression. And so, in one of the most influential books on anatomy "de humani corporis fabrica" (1543), Galenus' theory of black bile as the explanation for cancer was finally dispelled [2].

This radical change in modern medicine was followed by Italian anatomist Giovanni Morgagni (1682–1771), who laid the foundations for scientific oncology by performing autopsies and relating the patient's illness to the pathology found after death. Scottish surgeon John Hunter (1728–1793) suggested that some cancer could be cured with surgery and described how the surgeon should decide upon which cancers to operate [3]. The invention of anesthesia in the nineteenth century allowed the practice of oncological surgery to flourish and physicians to develop standard surgical approaches. In 1871, the Austrian surgeon Theodor Billroth performed the first esophagectomy, followed in 1873 by the first laryngectomy and most famously, the first gastrectomy in 1881 [4]. The first pancreaticoduodenectomy was performed in 1898 by the Italian surgeon Alessandro Codivilla. American surgeon Allen Whipple refined the technique in 1935 to the procedure commonly referred to as the Whipple-procedure. By the late nineteenth century, several surgeons also started to perform elective resections of liver tumors. However, without knowledge of the segmental anatomy of the liver, these were all based on random resections resulting in extremely high mortality rates. In 1952 Jean-Louis Lortat-Jacob performed the first elective hepatic resection that was based on the segmental anatomy described by Couinaud [5]. By the late 1970s, the overall survival benefit of hepatic resection of colorectal liver metastases (CRLM) was established. Couinaud's anatomic knowledge, combined with advances in anesthesia and antiseptics, resulted in an impressive reduction of complications: mortality rates dropped from around 20% during the mid-1960s to 2–3% during the early 1990s.

The twentieth century also saw the emergence of two other mainstays of cancer therapy: systemic chemotherapy and external beam radiation therapy. In 1943, a German air raid in Bari, Italy, led to the destruction of 17 American warships. One of the ship's secret cargo consisted of 70-ton mustard gas bombs to be used in the battlefield. When the ship exploded, the deadly load dispersed into the air. The dissemination of the gas to the nearby harbor of Bari resulted in the death of almost a thousand people in the months following the explosion. Stewart Francis Alexander, a Lieutenant Colonel and an expert in chemical warfare, investigated the aftermath. Autopsies of the victims suggested that profound lymphoid and myeloid suppression had developed after exposure. In his

report, Alexander theorized that since mustard gas all but ceased the division of certain types of somatic cells whose nature was to divide fast, it could also potentially be put to use in helping to suppress the division of certain types of cancerous cells [6]. Using this information, two pharmacologists from the Yale School of medicine, Louis Goodman and Alfred Gilman, injected mustine, a related agent (the prototype nitrogen mustard anticancer chemotherapeutic) into a patient with non-Hodgkin's lymphoma. They observed a dramatic reduction in the patient's tumor masses [7]. Although the effect lasted only a few weeks, this was the first step to the realization that cancer could be treated by pharmacological agents [8]. This success was soon followed by Sidney Farber, often named the father of chemotherapy, who was the first to achieve a remission in a child with acute myeloid leukemia using the folic acid-antagonist aminopterin in 1948 [2]. After this discovery, an extensive search for other chemotherapeutic agents began, and many different chemotherapeutics were developed. The early chemotherapy regimens were life-threatening procedures and resulted in a temporary response at best, but some of these agents are still in use. For example, fluorouracil (5-FU), still one of the mainstays of chemotherapy for colorectal liver metastases, was first described in 1957. Recently, targeted therapies such as kinase inhibitors and monoclonal antibodies have been added to the arsenal of systemic therapies.

In 1895, Wilhelm Conrad Röntgen discovered the basic properties of ionizing radiation (X-rays) and the possibility of using radiation in medicine. During early practical work and scientific investigation, experimenters noticed that prolonged exposure to X-rays created inflammation and, more rarely, tissue damage on the skin. Emil Grubbe, a medical student, hypothesized that the destruction of skin as a side effect of radiation could be used to treat tumors. On March 29, 1896, he bombarded the breast of an aged lady, Rose Lee, in which a painful recurrence after mastectomy had developed. The treatment resulted in significant tumor shrinkage. This first radiation treatment indicated the foundation of the field of radiation oncology [9]. The discovery of Radium in 1898 by Marie Curie resulted in the speculation whether it could be used for therapy in the same way as X-rays. Radium was soon seen as a way to treat disorders that were not affected enough by X-ray treatment because it could be applied in a multitude of ways in which X-rays could not [10]. By the 1930s, radiation oncologists were able to achieve permanent remission of several types of cancer in a significant fraction of patients. Further improvement came with the introduction of megavoltage linear accelerators in the 1950s. Nowadays, the three main divisions of radiation therapy are external beam radiation therapy, brachytherapy, and systemic radioisotope therapy. The past years, a more precise method of external beam radiation has been developed: stereotactic ablative radiotherapy (SABR). SABR refers to highly focused radiation treatment, delivering an intense dose concentrated on the tumor with submillimeter accuracy, while limiting the dose to the surrounding organs. SABR is increasingly used to treat lung, liver, brain, and pancreatic tumors (Fig. 1.1).

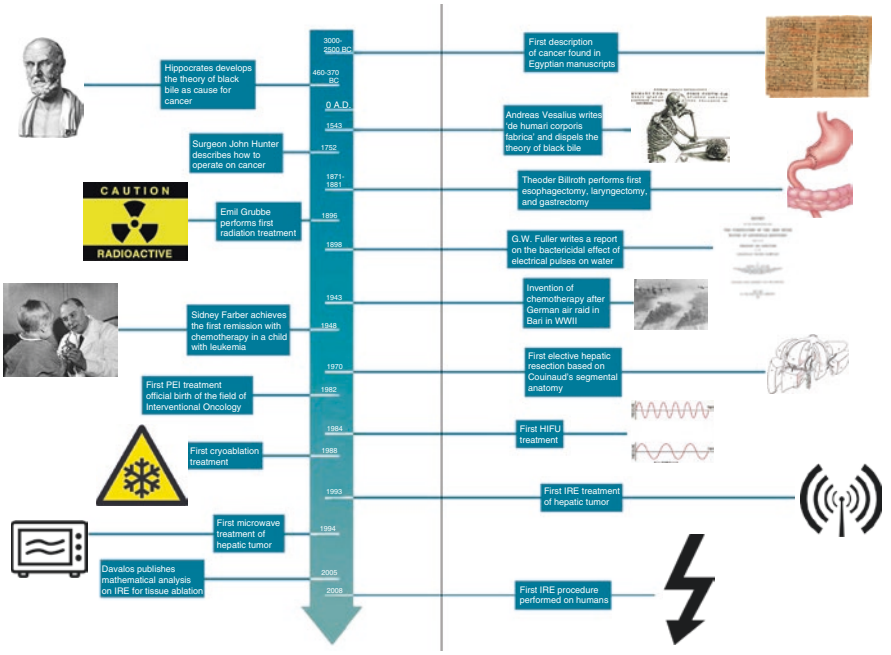

Fig. 1.1 Historical landmarks in oncology

1.2 Image-Guided Tumor Ablation: A Brief History

Decades of intensive cancer research have resulted in continuously improved surgical, chemotherapeutic, and radiation treatments. This has led to a dramatic improvement in overall cancer survival. However, despite the advances of surgical techniques, many tumors are still considered unsuitable for surgical resection, especially primary and secondary liver tumors; for example, only 20–30% of the patients with CRLM are found eligible for surgery because of unfavorable tumor location, disease extent or insufficient hepatic reserve, and comorbidity [11]. The use of radiotherapy for liver tumors is traditionally limited due to the low tolerance of normal liver tissue to radiation, which results in radiation-induced liver disease in a significant proportion of patients [12]. Furthermore, although it greatly improves overall survival, chemotherapy generally has a temporary effect and rarely leads to complete regression on its own.

1.2.1 Percutaneous Ethanol Ablation

In order to be able to treat some of these unresectable tumors, forward thinking surgeons, radiologists, and interventional radiologists started to consider and realize the potential to treat solid tumors using a completely new modality: “tumor ablation”,

with the help of electrodes or probes inserted into tumors, delivering chemicals or energy in order to achieve local control. Historically, percutaneous ethanol injection (PEI) was the first percutaneous ablative therapy to be clinically applied in the early 1980s. Ethanol causes thrombosis and disruption of the endothelium of small blood vessels and induces cell death due to dehydration. The official birth of percutaneous interventional oncology was marked by the first papers on PEI of small hepatic and abdominal tumors and parathyroid hyperplasias [13, 14]. In two subsequent papers, Livraghi and Ebara and colleagues demonstrated PEI to be cheap, safe, and effective in the treatment of hepatocellular carcinoma (HCC) [15, 16]. However, in the treatment of metastatic disease PEI proved less effective, since the heterogeneous and often fibrous nature of metastatic tumors restricts the diffusion of ethanol. For a similar reason, other injectable agents such as chemotherapeutic drugs and hot saline did not provide great efficacy for the treatment of metastatic liver disease. Different methods for ablation based on the deposition of physical energy therefore came into being.

1.2.2 Radiofrequency Ablation

Of the different ablation techniques, radiofrequency ablation (RFA) is currently the most widely employed technique. While the clinical use of RFA is relatively new, the biological effects of radiofrequency currents were already recognized long before their therapeutic use was investigated. In 1891, D'Arsonval demonstrated that when radiofrequency waves passed through tissue, they caused an increase in tissue temperature [17]. In 1910, the British urologist Edwin Beer described a new method for the treatment of bladder neoplasms using cauterization through a cystoscope [18], followed in 1911 by William Clark who described the use of oscillatory desiccation in the treatment of malignant tumors that were accessible for minor surgical procedures [19]. However, presumably because of the lack of image guidance, it was not until 1990 that two independent investigators, McGahan and Rossi, used a modification of prior radiofrequency techniques to create coagulation via the percutaneous route using specifically designed needles [20, 21]. In 1993 this technique was used for the first time to ablate liver tumors in humans [22]. RFA uses a needle applicator that emits an alternating electric current, which results in the generation of heat and ultimately protein denaturation resulting in cell death. Over the past 10 years, manufacturers have designed more powerful generators, developed special programs for heat deposition, and improved needle designs such as the deployable prongs and the saline-cooled applicator, which caused less tissue charring, both considerably increasing coagulation volumes. Nowadays, RFA has reached a high level of reliability for the treatment of HCCs up to 5–6 cm in size, of hepatic metastases up to 3–4 cm and, of some extrahepatic malignancies, such as lung, kidney, and bone neoplasms [23–26].

1.2.3 High-Intensity Focused Ultrasound

High-intensity focused ultrasound (HIFU) represents another thermal tumor ablation technique. The biological effects of ultrasound were known long before its use for diagnostic imaging was proposed. During the First World War, the French physicist Paul Langevin worked on a detection method for submarines. He reported that "fish placed in the beam in the neighborhood of the source operating in a small tank were killed immediately, and certain observers experienced a painful sensation on plunging the hand in this region". In 1942, John Lynn was the first to use HIFU to create focal ablation lesions in vivo. In the late 1950s, William and Francis Fry developed a four-element HIFU transducer which was used for the first clinical HIFU treatments of Parkinsonism and hyperkinesis in 1958 by Russell Meyers. In the late 1980s, when ultrasound imaging became widely available, US-HIFU was intensely investigated for the ablation of liver tumors. In 1993, Hynynen and coworkers proposed the use of magnetic resonance (MR) for therapy guidance. The combination of MR guidance and HIFU ablation was coined MR-HIFU and marked the beginning of a renewed interest in this treatment modality.

1.2.4 Cryoablation

Extremely cold temperatures have been used to decrease inflammation and to relieve pain since the time of the ancient Egyptians. In the nineteenth century an English physician, James Arnott, used a combination of ice and salt to produce tissue necrosis for tumors of the cervix and breast by topic application [27]. Liquid air and carbon dioxide were subsequently employed as cryogens for the treatment of tumors, based on the principle used for air conditioning and refrigeration; atmospheric gases warm when compressed and cool during expansion. Following many experimental studies using liquid nitrogen as cryogen [28], the first clinical experiences with the use of cryotherapy were reported by the late 1980s. The key development was the fusion of cryoablation with real-time image guidance to verify the extent of treatment and to measure the size of the ice ball created by freezing [29]. Interstitial hepatic cryosurgery initially started as an intraoperative procedure, mostly because of the large size of cryoprobes. Thanks to the subsequent development of argon-based cryoablation systems with much thinner cryoprobes and decreased treatment times, minimally invasive cryoablation techniques, including the percutaneous approach under cross-sectional image guidance, have been introduced for – predominantly – kidney, lung, and bone malignancies [30].

1.2.5 Laser Ablation

Laser ablation (or laser-induced interstitial thermotherapy) uses laser for thermal tumor destruction. The neodymium: yttrium-aluminum-garnet (Nd: YAG) laser system was initially used to treat head and neck tumors through precise surgical

dissections rather than for tumor destruction. The first experimental application of laser hyperthermia for the treatment of liver neoplasms was reported in 1987 [31]. Recent improvements in laser-induced thermotherapy allow larger areas of coagulative necrosis than the earlier systems [32, 33]. However, the clinical acceptance of laser ablation has been limited, in part due to the technical complexity of the method requiring several fiber placements compared to the other easier-to-perform thermal ablation methods.

1.2.6 Microwave Ablation

Microwave ablation (MWA) is the most recently introduced thermal ablation technique. It uses a monopolar antenna causing water molecules in the tissue to vibrate at a higher frequency than with RFA. This generates frictional heat in the water molecules and leads to thermal coagulation of tissue. The first reports about US-guided percutaneous MWA for the treatment of unresectable HCC were published in 1994 [34]. Microwave energy has demonstrated several advantages over RFA [35]. Microwaves readily penetrate through biologic materials, including those with low electrical conductivity, such as lung, bone, and dehydrated or charred tissue. Consequently, microwave power can produce continuous, extremely high (>150 °C) temperatures, which improves ablation efficacy by increasing thermal conduction into the surrounding tissue. Multiple antennas can be operated simultaneously [36–38]. On the other hand, the distribution of microwave energy is inherently more difficult to control, which can lead to unintended injuries to other tissues [39, 40].

Modern approaches take advantage of the vastly superior armamentarium of imaging strategies nowadays available. Advances in the technique combined with improved localization now make it possible to be much more aggressive and effective in attempting to achieve local control of unresectable primary or metastatic tumors. Ablative therapies have gained widespread attention and, in many cases, broad clinical acceptance as methods for treating focal malignancies in a wide range of tumor types and tissues, including primary and secondary malignancies of the liver, kidney, lung, and bone [35, 41–44]. Each minimally invasive ablation technique has their own advantages and disadvantages and particular applications [45]. However, all the currently used effective ablative modalities are thermal techniques. Because these methods depend on thermal injury, they inadvertently carry some risk of damage to the adjacent extracellular environment like blood vessels and bile ducts, which can lead to serious complications. Other common complications of thermal ablation are perforation of adjacent bowel structures or the diaphragm. Another disadvantage of thermal ablation is that the extent of the treated area is difficult to control because blood circulation has a strong local effect on the distribution of heat. As a result, temperatures near large vessels decrease, which can lead to incomplete ablation of tumors located near these vessels. Due to this so-called heat-sink effect, the chance of complete ablation is effectively decreased to up

to 50% for RFA near large vessels. In recent years, a new method of tumor ablation has emerged that addresses the limitations of thermal ablation: irreversible electroporation.

References

1. Breasted JH. The Edwin Smith surgical papyrus: published in facsimile and hieroglyphic transliteration with translation and commentary in two volumes. Chicago: University of Chicago Press, University of Chicago Oriental Institute Publications; 1991.
2. Mukherjee S. The emperor of all maladies: a biography of cancer. New York: Scribner; 2011.
3. Moore W. The knife man: the extraordinary life and times of John Hunter, father of modern surgery. London: Bantam Press; 2005.
4. Nuland B. Doctors: the biography of modern medicine. New York: Knopf; 1988.
5. Lortat-Jacob J, Robert H. Well defined technique for right hepatectomy. Paris: La presse medicale; 1952.
6. Li JJ. Laughing gas, viagra and lipitor: the human stories behind the drugs we use. New York: Oxford University Press; 2006.
7. Gilman A. The initial clinical trial of nitrogen mustard. Am J Surg. 1963;105:574–8.
8. Fenn J, Udelsman R. First use of intravenous chemotherapy cancer treatment: rectifying the record. J Am Coll Surg. 2011;212(3):413–7.
9. MacKee GM. X-rays and radium in the treatment of diseases of the skin. Philadelphia: Lea & Febiger; 1921.
10. Metzenbaum M. Radium: its value in the treatment of lupus, rodent ulcer, and epithelioma, with reports of cases. Int Clin. 1905;4(14):21–31.
11. Leporrier J, Maurel J, Chiche L, Bara S, Segol P, Launoy G. A population-based study of the incidence, management and prognosis of hepatic metastases from colorectal cancer. Br J Surg. 2006;93:465–74.
12. Emami B, Lyman J, Brown A. Tolerance of normal tissue to therapeutic irradiation. Int J Radiat Oncol Biol Phys. 1991;21:109–22.
13. Solbiati L, Giangrande A, De Pra L, Bellotti E, Cantu P, Ravetto C. Percutaneous ethanol injection of parathyroid tumours under US guidance: treatment for secondary hyperparathyroidism. Radiology. 1985;155:607–10.
14. Livraghi T, Festi D, Monti F, Salmi A, Vettori C. US-guided percutaneous ethanol injection of small hepatic and abdominal tumours. Radiology. 1986;161:309–12.
15. Livraghi T, Salmi A, Bolondi L, Marin G, Arienti V, Monti F. Small hepatocellular carcinoma: percutaneous alcohol injection – results in 23 patients. Radiology. 1988;1(168):313–7.
16. Ebara M, Otho M, Sugiura N, Okuda K, Kondo F, Kondo Y. Percutaneous ethanol injection for the treatment of small hepatocellular carcinoma: study of 95 patients. J Gastroenterol Hepatol. 1990;5:616–25.
17. D'Arsonval M. Action physiologique des courants alternatifs. C R Soc Biol. 1891;43:283–6.
18. Beer E. Removal of neoplasms of the urinary bladder. A new method employing frequency (Oudin) currents through a catheterizing cystoscope. JAMA. 1910;54:1768.
19. Clark W. Oscillatory desiccation in the treatment of accessible malignant growths and minor surgical conditions. J Adv Ther. 1911;29:169–83.
20. McGahan J, Browning P, Brock J, Tesluk H. Hepatic ablation using radiofrequency electrocautery. Investig Radiol. 1990;25:267–70.
21. Rossi S, Fornari F, Pathies C, Buscarini L. Thermal lesions induced by 480 KHz localized current field in guinea pig and pig liver. Tumori. 1990;76:54–7.
22. McGahan J, Schneider P, Brock J, Tesluk H. Treatment of liver tumors by percutaneous radiofrequency electrocautery. Semin Interv Radiol. 1993;10:143–9.

23. Solbiati L, Livraghi T, Goldberg S. Percutaneous radiofrequency ablation of hepatic metastases from colorectal cancer: long-term results in 117 patients. Radiology. 2001;221:159–66.
24. Belfiore G, Moggio G, Tedeschi E. CT-guided radiofrequency ablation: a potential complementary therapy for patients with unresectable primary lung cancer – a preliminary report of 33 patients. AJR Am J Roentgenol. 2004;183:1003–11.
25. Mayo-Smith W, Dupuy D. Adrenal neoplasms: CT-guided radiofrequency ablation. Preliminary results. Radiology. 2004;231:225–30.
26. Rosenthal D, Hornicek F, Torriani M, Gebhardt M, Mankin H. Osteoid osteoma: percutaneous treatment with radiofrequency energy. Radiology. 2003;229:171–5.
27. Gage A. History of cryosurgery. Semin Surg Oncol. 1998;14:99–109.
28. Dutta P, Montes M, Gage A. Large volume freezing in experimental hepatic cryosurgery. Avoidance of bleeding in hepatic freezing by an improvement in the technique. Cryobiology. 1979;16:50–5.
29. Ravikumar T, Kane R, Cady B. Hepatic cryosurgery with intraoperative ultrasound monitoring for metastatic colon carcinoma. Arch Surg. 1987;122:403.
30. Permpongkosol S, Nielsen M, Solomon S. Percutaneous renal cryoablation. Urology. 2006;68:19–25.
31. Hashimoto D. Application of the laser thermal effect to the therapy of liver neoplasms. Nippon Rinsho. 1987;45:888–96.
32. Pacella C, Bizzarri G, Francica G. Percutaneous laser ablation in the treatment of hepatocellular carcinoma with small tumours: analysis of factors affecting the achievement of tumour necrosis. J Vasc Interv Radiol. 2005;16:1447–57.
33. Vogl T, Straub R, Eichler K, Sollner O, Mack M. Colorectal carcinoma metastases in liver: laser-induced interstitial thermotherapy – local tumour control rate and survival data. Radiology. 2004;230:450–8.
34. Seki T, Kubota Y, Wakabayashi M. Percutaneous transhepatic microwave coagulation therapy for hepatocellular carcinoma proliferating in the bile duct. Dig Dis Sci. 1994;39:663–6.
35. Ahmed M, Brace CL, Lee FT, Goldberg SN. Principles of and advances in tumor ablation. Radiology. 2011;258(2):351–69.
36. Brace C, Laeseke P, Sampson L, Frey T, van der Weide D, Lee FJ. Microwave ablation with a single small-gauge triaxial antenna: in vivo porcine liver model. Radiology. 2007;242:435–40.
37. Goldberg S, Hahn P, Tanabe K. Percutaneous radiofrequency tissue ablation: does perfusion-mediated tissue cooling limit coagulation necrosis? J Vasc Interv Radiol. 1998;9:101–11.
38. Ahmed M, Lobo S, Weinstein J. Improved coagulation with saline solution pretreatment during radiofrequency tumor ablation in a canine model. J Vasc Interv Radiol. 2002;13:717–24.
39. Strickland A, Clegg P, Cronin N. Experimental study of large-volume microwave ablation in the liver. Br J Surg. 2002;89:1003–7.
40. Wolf F, Grand D, Machan J, Dipetrillo T, Mayo-Smith W, Dupuy D. Microwave ablation of lung malignancies: effectiveness, CT findings, and safety in 50 patients. Radiology. 2008;247:871–9.
41. Gillams AR, Lees WR. Five-year survival in 309 patients with colorectal liver metastases treated with radiofrequency ablation. Eur Radiol. 2009;19(5):1206–13.
42. Livraghi T, Solbiati L, Meloni M, Gazelle G, Halpern E, Goldberg S. Treatment of focal liver tumors with percutaneous radio-frequency ablation: complications encountered in a multicenter study. Radiology. 2003;226(2):441–51.
43. Dupuy D, DiPetrillo T, Gandhi S, Ready N, Ng T, Donat W, et al. Radiofrequency ablation followed by conventional radiotherapy for medically inoperable stage I non-small cell lung cancer. Chest. 2006;129(3):738–45.
44. Gervais D, McGovern F, Arellano R, McDougal W, Mueller P. Renal cell carcinoma: clinical experience and technical success with radio-frequency ablation of 42 tumors. Radiology. 2003;226(2):417–24.
45. Davalos RV, Mir LM, Rubinsky B. Tissue ablation with irreversible electroporation. Ann Biomed Eng. 2005;33(2):223–31.