

## Radiofrequency Ablation of Breast Cancer: First Report of an Emerging Technology [Original Article]

Jeffrey, Stefanie S. MD; Birdwell, Robyn L. MD; Ikeda, Debra M. MD; Daniel, Bruce L. MD; Nowels, Kent W. MD; Dirbas, Frederick M. MD; Griffey, Stephen M. DVM, PhD

From the Departments of Surgery (Drs Jeffrey and Dirbas), Radiology (Drs Birdwell, Ikeda, and Daniel), and Pathology (Dr Nowels), Stanford University School of Medicine, Stanford, Calif; and the Comparative Pathology Laboratory, School of Veterinary Medicine, University of California, Davis (Dr Griffey). Dr Ikeda has stock in a venture capital corporation that has a small amount of stock in RadioTherapeutics Corp, Mountain View, Calif.

Reprints: Stefanie S. Jeffrey, MD, Medical School Office Building X-300, Stanford Medical Center, Stanford, CA 94305-5414 (e-mail: stefanie.jeffrey@stanford.edu).



### Outline

- [Abstract](#)
- [PATIENTS, MATERIALS, AND METHODS](#)
- [RESULTS](#)
- [COMMENT](#)
- [References](#)

### Graphics

- [Figure 1](#)
- [Figure 2](#)
- [Figure 3](#)
- [Figure 4](#)
- [Figure 5](#)
- [Figure 6](#)

### Output...

- [Print Preview](#)
- [Email Article Text](#)
- [Save Article Text](#)

### Links...

- [About this Journal](#)
- [Abstract Complete Reference](#)
- [Help](#)
- [Logoff](#)

### History...

Radiofrequency Ablation o...

### Abstract

**Hypothesis:** Radiofrequency (RF) energy applied to breast cancers will result in cancer cell death.

**Design:** Prospective nonrandomized interventional trial.

**Setting:** A university hospital tertiary care center.

**Patients:** Five women with locally advanced invasive breast cancer, aged 38 to 66 years, who were undergoing surgical resection of their tumor. One patient underwent preoperative chemotherapy and radiation therapy, 3 patients received preoperative chemotherapy, and 1 had no preoperative therapy. All patients completed the study.

**Interventions:** While patients were under general anesthesia and just before surgical resection, a 15-gauge insulated multiple-needle electrode was inserted into the tumor under sonographic guidance. Radiofrequency energy was applied at a low power by a preset protocol for a period of up to 30 minutes. Only a portion of the tumor was treated to evaluate the zone of RF ablation and the margin between ablated and nonablated tissue. Immediately after RF ablation, the tumor was surgically resected (4 mastectomies, 1 lumpectomy). Pathologic analysis included hematoxylin-eosin staining and enzyme histochemical analysis of cell viability with nicotinamide adenine dinucleotide–diaphorase (NADH–diaphorase) staining of snap-frozen tissue to assess immediate cell death.

**Main Outcome Measure:** Cancer cell death as visualized on hematoxylin-eosin–stained paraffin section and NADH–diaphorase cell viability stains.

**Results:** There was evidence of cell death in all patients. Hematoxylin-eosin staining showed complete cell death in 2 patients. In 3 patients there was a heterogeneous pattern of necrotic and normal-appearing cells within the ablated tissue. The ablated zone extended around the RF electrode for a diameter of 0.8 to 1.8 cm. NADH–diaphorase cell viability stains of the ablated tissue showed complete cell death in 4 patients. The fifth patient had a single focus of viable cells (<1 mm) partially lining a cyst. There were no perioperative complications related to RF ablation.

**Conclusions:** Intraoperative RF ablation results in invasive breast cancer cell death. Based on this initial report of the use of RF ablation in breast cancer, this technique merits further investigation as a percutaneous minimally invasive modality for the local treatment of breast cancer.

Arch Surg.1999;134:1064-1068

---

IN RECENT years, there has been a transition toward less invasive local treatment of breast cancer. The shift from radical mastectomy 2-3 and modified radical mastectomy 4-7 to breast conservation therapy 8-15 has not altered survival rates. Following this continuum, investigators are studying percutaneous minimally invasive techniques to locally eradicate breast tumors. Cryoablation, 16-17 laser ablation, 18 and high-intensity focused ultrasound 19-20 have been reported for ablation of benign and malignant breast lesions. Radiofrequency (RF) energy heats tissue, causing thermal destruction and cell death by coagulation necrosis. This technique has been used for ablation of liver, prostate, bone, and renal tumors; pharyngeal soft tissue; neural tissue; and brain lesions. 21-27 We report the first series of RF ablation in patients with breast cancer.

## **PATIENTS, MATERIALS, AND METHODS**

Five women with locally advanced (stage III) breast cancer or tumors larger than 5 cm who were scheduled to undergo surgical resection volunteered for this study with the understanding that the ablation procedure would not change their clinical management. All signed an institutional review board–approved informed consent. Women with large tumors were selected to determine the extent of tissue destruction by RF energy applied to a single site within the tumor. Preoperative diagnosis of ductal carcinoma was made by fine needle aspiration biopsy in 2 patients and core needle biopsy in 3 patients. Three of the 5 women underwent preoperative chemotherapy with varying clinical responses, 1 underwent preoperative chemotherapy and radiation therapy, and 1 had no preoperative therapy. At the time of the RF ablation procedure, tumor size ranged from 4 to 7 cm as measured by clinical examination or mammography.

General anesthesia was induced in all 5 patients. The breast was prepared and draped under sterile conditions. The tumor site was identified by intraoperative sonography using the ATL HDI 3000 system (Advanced Technology Laboratories, Bothell, Wash) with a broadband 9- to 5-mHz linear transducer. The skin overlying the tumor was nicked with an 11-blade, and a 15-gauge insulated multiple-needle electrode (LeVeen needle electrode; RadioTherapeutics Corp, Mountain View, Calif)

was inserted into a single site within the tumor under direct sonographic guidance. Radially spaced stainless steel wires that spread outward in an inverted arc with a tip-to-tip diameter of 2 cm were deployed (Figure 1). The multiple-needle electrode was connected to the RF-2000 generator (RadioTherapeutics Corp), and a return electrode pad (Valley Lab, Boulder, Colo) on the patient was connected to complete the current path. After the protocol was in progress, a decision was made to add temperature monitoring data. In the final 3 patients, a 21-gauge temperature probe (Brymill Cryogenic Systems, Ellington, Conn) was inserted into the tumor adjacent to the base of the wire array.

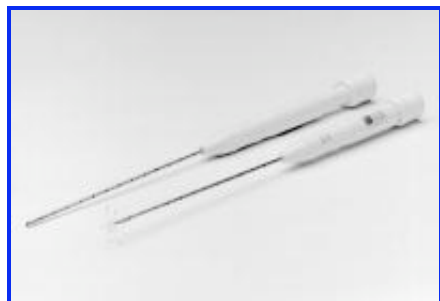


Figure 1. Multiple-needle electrode for radiofrequency ablation. Radially spaced wires extend from deployed needle.

[\[Help with image viewing\]](#)

By using a predetermined standardized algorithm, RF energy was applied in 2 time periods, not to exceed a total of 30 minutes. The maximum time of 30 minutes was chosen to avoid an indefinite delay in operative time. In the first time period, power was initially set to 12 to 15 W. After 10 minutes, power was increased in 5-W steps until a rapid rise in impedance (ohms) occurred, indicating tissue desiccation, or until 15 minutes was reached. In the second time period, power was restarted at 75% of the previously determined highest power setting before the increase in impedance, or continued at the last setting if the first 15-minute time limit was attained. Ten minutes into the second time period, power was again increased in 5-W steps to a maximum of 60 W or until 15 minutes elapsed. Temperature recordings were made during RF ablation in the last 3 patients, but did not affect the power setting algorithm. Ice packs were placed on the breast before applying RF energy and for the duration of the ablation procedure to minimize possible thermal injury to the skin.

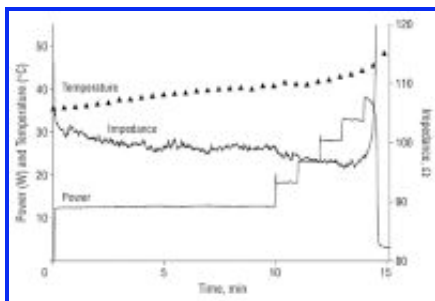
Following RF ablation, the multiple-needle electrode was disconnected and cut with a wire cutter at the skin. Four of the 5 women underwent modified radical mastectomy and 1 underwent lumpectomy and axillary lymph node excision. The breast tissue was immediately sent to the pathology laboratory and margins were inked. The breast tissue was incised from the posterior aspect until the tissue surrounding the needle electrode was identified. This tissue was divided and a representative section of tumor and surrounding tissue from each case was immediately placed in OCT compound embedding medium (Tissue-Tek; Sakura Finetek USA Inc, Torrance, Calif), snap-frozen in liquid nitrogen, and stored at  $-70^{\circ}\text{C}$  for cell viability staining with nicotinamide adenine dinucleotide–diaphorase (NADH-diaphorase). Frozen samples were sent on dry ice to a collaborating laboratory. Adjacent tissue was fixed in formalin, embedded in paraffin, sectioned, and stained with hematoxylin-eosin (H&E).

The enzyme histochemical analysis of cell viability technique used in this study is based on the reduction of nitroblue tetrazolium chloride, a redox indicator, by NADH-diaphorase, resulting in an intense blue cytoplasmic pigment. The activity of this enzyme has been shown to subside immediately upon cell death. <sup>28</sup> For enzyme histochemical analysis of cell viability, 8- $\mu\text{m}$  cryostat-cut unfixed sections were placed on glass slides. Incubation media consisted of 1 mL of reduced [ $\alpha$ ]-NADH (Sigma-Aldrich

Corporation, St Louis, Mo) at a concentration of 2.5-mg/mL distilled water, 2.5-mL nitroblue tetrazolium chloride (Sigma-Aldrich Corporation) at a concentration of 2-mg/mL distilled water, 1 mL of phosphate-buffered saline (pH 7.4) at a concentration of 2 mg/mL, and 0.5 mL of Ringer solution. Each tissue section slide was covered with 100  $\mu$ L of incubation media for 15 minutes under aerobic conditions at room temperature. Each slide was then washed in distilled water for 2 minutes. Glass cover slips were then mounted with an aqueous medium. Slides were evaluated for characterization of staining within 24 hours of processing. A section of normal liver was used as a positive control, and a section of normal liver placed in phosphate-buffered saline and heated to 100°C was used as a negative control.

## RESULTS [↑](#)

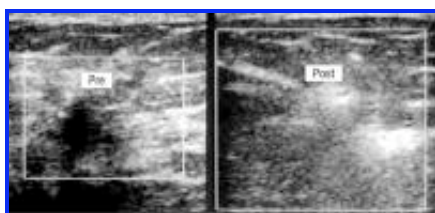
The application of RF energy in breast cancer tissue resulted in a tissue temperature rise from baseline temperatures of 35.4°C, 35.3°C, and 36.1°C to maximum tissue temperatures of 46.8°C, 51.3°C, and 70.0°C, respectively, in the 3 patients in which it was measured. Continuous recordings were made of the power applied and tissue impedance (a measure of resistance to flow of electrical current). As tissue desiccation occurred, impedance increased more than 10-fold, with a precipitous decline in power. In 4 of the 5 patients, this increase in impedance and reciprocal decrease in power was observed between 12 and 28 minutes ([Figure 2](#)). An average of 36 W (range, 20-60 W) was necessary to achieve tissue desiccation in these 4 patients. In 1 patient, RF ablation was terminated at the preset 30-minute time limit before achieving the tissue desiccation necessary for an exponential increase in impedance and decrease in power. Like 2 other patients in the study, this patient had received preoperative chemotherapy only; she did not undergo preoperative radiation therapy. It is not evident why the rise in impedance and decrease in power did not occur in this patient within the predetermined 30-minute time interval as it did in others.



[\[Help with image viewing\]](#)

Figure 2. In vivo radiofrequency ablation of breast tissue. Graph shows changes in breast cancer tissue impedance and temperature during creation of a thermal lesion by radiofrequency energy. Power was initially set to 12 W and after 10 minutes was increased in 5-W steps. After 14½ minutes, power decreased rapidly as impedance exponentially increased due to tissue desiccation. Tissue temperature increased from body temperature to a level sufficient to cause cell death.

During tumor ablation, continuous sonographic imaging demonstrated gradual changes in the heated tissue around the electrode. Well-defined, clearly marginated hypoechoic regions became less distinct with an increase in overall echogenicity ([Figure 3](#)).



[\[Help with image viewing\]](#)

Figure 3. Intraoperative breast sonogram before (Pre) and immediately after (Post) radiofrequency ablation demonstrates increasing echogenicity of the ablated tumor.

On gross examination, there was no visible difference between ablated tissue and surrounding tissue. However, the treated tissue was palpably firmer than the untreated tissue. Microscopic examination of the treated tissue with H&E stains demonstrated well-defined areas of characteristic cautery or heating effect evidenced by pyknotic nuclei and increased intensity of eosinophilic staining (Figure 4), extending for a diameter of 0.8 to 1.8 cm. In the RF ablation zone, all cells were necrotic in 2 patients; normal-appearing cells were interspersed between necrotic cells in 3 patients.

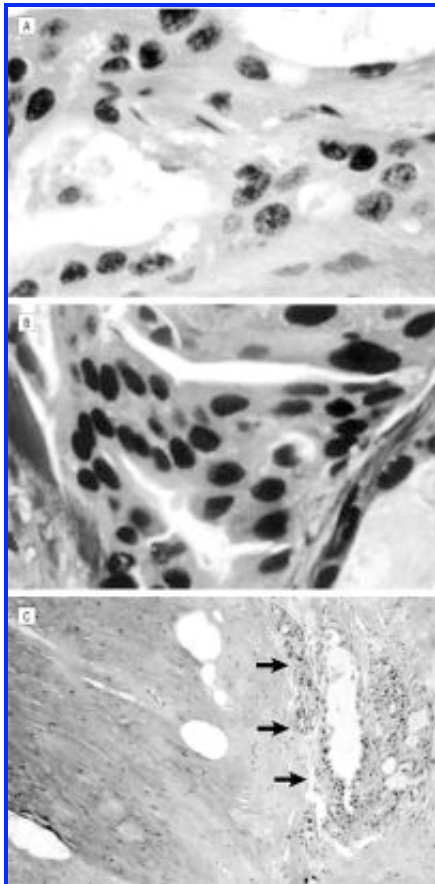


Figure 4. Photomicrographs of breast tissue after radiofrequency ablation. A, Breast carcinoma away from ablated area, showing viable cancer cells (hematoxylin-eosin,  $\times 400$ ). B, Thermal ablation of breast cancer cells showing pyknotic nuclei and increased intensity of eosinophilic stroma (hematoxylin-eosin,  $\times 400$ ). C, Low-power photomicrograph of zone (arrows) between nonviable and viable tissue (hematoxylin-eosin,  $\times 100$ ).

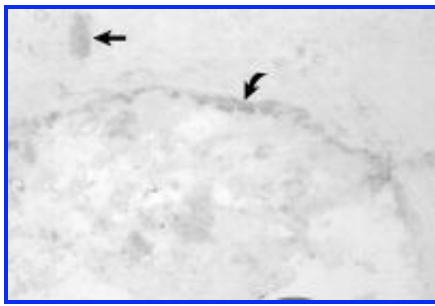
[\[Help with image viewing\]](#)

Enzyme histochemical analysis of cell viability by NADH-diaphorase showed no staining of cells in the RF-ablated region in 4 patients, consistent with complete loss of cell viability (Figure 5). One patient had a single area of cell viability within a cyst wall, measuring less than 1 mm (Figure 6).



Figure 5. Staining of ablated tissue demonstrates no viable cells (nicotinamide adenine dinucleotide-diaphorase,  $\times 125$ ).

[\[Help with image viewing\]](#)



[\[Help with image viewing\]](#)

Figure 6. Staining of ablated breast tissue demonstrates a rim of viable epithelial cells (curved arrow) lining approximately 40% of a cyst circumference and measuring less than 1 mm (nicotinamide adenine dinucleotide–diaphorase,  $\times 125$ ). Under the microscope, blue intracytoplasmic staining is demonstrated within the cystic epithelial cells; other dark clumps of tissue outside the cyst (straight arrow) appear brown.

Postoperatively, surgical wounds healed without infection or evidence of skin burn in all patients. One patient who underwent preoperative chemotherapy and radiation therapy required additional visits for percutaneous drainage of residual chest wall seroma after mastectomy drains were removed.

## COMMENT [↑](#)

Surface and percutaneous minimally invasive techniques were used to treat breast cancer as early as the mid-19th century. Freezing techniques with iced saline solutions were used to decrease the pain of advanced breast tumors. [29](#) Electric current delivered through needles inserted into breast tumors or given via clay electrodes on the skin reportedly relieved breast cancer pain and, in some cases, resulted in tumor shrinkage. [30](#)

There has been a recent resurgence of interest in percutaneous minimally invasive tissue ablation. Successful tissue destruction has been reported using cryotherapy, laser therapy, high-intensity focused ultrasound, and RF ablation. [16-27, 29, 31-32](#)

Although definitive studies of the efficacy of treating limited-stage breast cancer with these other techniques have not been performed, several limitations have been discovered that motivated our investigation of RF ablation as an alternative. Cryosurgery has variable tumoricidal efficacy. In prostate cancer treatment, residual tumor rates of 7% to 83% have been reported, depending on the freezing protocols used. [31-32](#) In experimental models of breast cancer, a single freeze-thaw cycle was associated with tumor recurrence rates in mice of 80%, and 5 freeze-thaw cycles were necessary to decrease recurrence rates to 5%. [16](#) There has been a single reported case of cryosurgery for breast cancer performed in a woman with 2 foci, 8 mm and 5 mm: tumor cell death was accomplished in both foci with 2 freeze-thaw cycles but follow-up was only 12 weeks. [17](#) Laser and focused ultrasound result in small-size ( $\leq 8$  mm) ablations, necessitating complex strategies to overlap multiple ablations to treat the majority of breast tumors. Radiofrequency ablation using a multiple-needle electrode has been demonstrated to be capable of achieving large-volume ablations (up to 3.5 cm in diameter) with complete cell death in other organ systems [21](#) in a reasonable amount of time ( $< 1/2$  hour). To date, however, no case has yet been reported of RF ablation for breast cancer.

During RF ablation, a high-frequency alternating current is delivered into tissue, causing excitation and motion of intracellular ions. This results in intracellular thermal heating by friction, [33](#) similar to electrosurgical coagulation (desiccation). Thermal injury to tissue starts at temperatures above  $41^{\circ}\text{C}$ , with the time of heat exposure necessary for complete cell death exponentially decreasing as temperature increases above  $42.5^{\circ}\text{C}$ . [34-36](#) Cell death is also affected by tissue type, phase in the cell cycle, pH, and blood flow. [34-36](#) At lower temperatures, apoptosis may be seen; at temperatures above  $46^{\circ}\text{C}$ , necrosis is identified, suggesting different temperature-related mechanisms of cell death. [35](#)

We have shown that it is feasible to use RF energy to ablate breast cancer. When tissue temperatures were recorded, temperatures above 46°C were achieved in all patients. Zones of cell death were clearly visible on H&E-stained sections, but in 3 patients, normal-appearing cells were interspersed between necrotic cells, suggesting incomplete cell death in the RF-ablated region. However, NADH-diaphorase viability stains are more accurate in determining extent of immediate cell death. Evaluation of tissue necrosis by this technique is less subjective than by routine H&E staining since interpretation is based on the presence or absence of intracytoplasmic blue pigment. <sup>28</sup> In the RF-ablated tissue, cells that appeared normal by H&E staining were nonviable by NADH-diaphorase staining. In our study design, we chose to ablate and then immediately resect the breast tissue while the patient was under general anesthesia. This is in contrast to the work of Mumtaz et al, <sup>18</sup> who performed interstitial laser photocoagulation of breast cancer under local anesthesia with a median interval between laser treatment and tumor removal of 5 days (range, 1-15 days). In the 2 cases in their study where NADH-diaphorase viability staining was performed, H&E findings of cell necrosis correlated directly with cell nonviability by NADH-diaphorase staining. It is possible that had we left ablated tissue in vivo for more than 24 hours (a treat, wait, and resect protocol), more accurate assessment of cell death by H&E staining would have been depicted.

There are significant unresolved issues when using in situ ablative technologies for local therapy. The first is that it is difficult to determine the extent of tissue necrosis in real time. Sonographic measurements are imprecise because of indistinct margins seen at the edges of the heated tissue. Preliminary investigations at our institution (unpublished data, 1997-?) suggest that ablation performed in the magnetic resonance therapy open magnet may more accurately predict the zone of necrosis. The data obtained from such experiments could then be correlated with sonographic and pathologic findings to allow translation back to a sonographically guided protocol. A second issue requiring further study is documentation of the resorption process for the ablated tissue—whether a palpable hard lump would persist that would be unsatisfactory for the patient and her medical providers or whether the tissue would revert to a more normal state. A third uninvestigated issue is the heterogeneity of breast tissue and breast cancer composition and its effect on the ablation process. Breast tissue may be fatty or dense, and breast cancers may show differing amounts of scirrhous (fibrotic) stroma. Since tissue impedance may differ, <sup>37</sup> protocols and monitoring techniques will need to be adapted accordingly to assure adequate central and circumferential tumor ablation. Factors such as tumor size, tissue conductivity, tissue perfusion, and tissue pH may affect the setting of ablation parameters. These may have played a role in our one patient who did not achieve the exponential rise in impedance and decrease in power within the 30-minute preset time period. Despite this, NADH-diaphorase stains did demonstrate complete tumor cell death in the ablated area in this patient.

An extremely important issue relates to assessing adequacy of tumor-free tissue margins. Initially this may be addressed with postablation percutaneous core biopsy sampling of breast tissue surrounding ablated tumor and close follow-up using multimodality breast imaging with mammography, ultrasound, and magnetic resonance imaging. Strict patient selection criteria should eliminate patients with multifocal and multicentric disease or diffuse calcifications that raise the question of extensive ductal carcinoma in situ. A prospective randomized trial will be necessary to demonstrate no increase in local recurrence rate following this procedure.

Percutaneous minimally invasive techniques for ablating breast tumors have potential benefit in that diseased tissue may be more selectively destroyed while leaving surrounding normal tissue in place. Radiofrequency ablation would be expected to be most applicable for tumors less than 3 cm, and it is likely that different size multiple-needle electrodes would be necessary to achieve different ablation

volumes. We believe that RF ablation of breast cancer merits further investigation.

A portion of salary support was provided to the Departments of Surgery, Radiology, and Pathology by RadioTherapeutics Corp, Mountain View, Calif, for conduct of this study. The processing and interpretation of the viability assay was paid for by RadioTherapeutics Corp to Comparative Pathology Laboratory Service, University of California, Davis.

We would like to acknowledge the editorial assistance of Sherry Wren, MD, in preparation of the manuscript.

## References

1. Fisher B. The evolution of paradigms for the management of breast cancer: a personal perspective. *Cancer Res.* 1992;52:2371-2383. [Bibliographic Links](#) [\[Context Link\]](#)
2. Halsted WS. The results of operations for the cure of cancer of the breast performed at the Johns Hopkins Hospital from June, 1889, to January, 1894. *Ann Surg.* 1894;20:497-555. [\[Context Link\]](#)
3. Halsted WS. The results of radical operations for the cure of carcinoma of the breast. *Ann Surg.* 1907;46:1-19. [\[Context Link\]](#)
4. Robinson GN, Van Heerden JA, Payne WS, Taylor WF, Gaffey TA. The primary surgical treatment of carcinoma of the breast: a changing trend toward modified radical mastectomy. *Mayo Clin Proc.* 1976;51:433-442. [Bibliographic Links](#) [\[Context Link\]](#)
5. Baker RR, Montague ACW, Childs JN. A comparison of modified radical mastectomy to radical mastectomy in the treatment of operable breast cancer. *Ann Surg.* 1979;189:553-559. [Bibliographic Links](#) [\[Context Link\]](#)
6. Turner L, Swindell R, Bell WGT, et al. Radical versus modified radical mastectomy for breast cancer. *Ann R Coll Surg Engl.* 1981;63:239-243. [Bibliographic Links](#) [\[Context Link\]](#)
7. Maddox WA, Carpenter JT Jr, Laws HL, et al. A randomized prospective trial of radical (Halsted) mastectomy versus modified radical mastectomy in 311 breast cancer patients. *Ann Surg.* 1983;198:207-212. [Bibliographic Links](#) [\[Context Link\]](#)
8. Recht A, Connolly JL, Schnitt SJ, et al. Conservative surgery and radiation therapy for early breast cancer: results, controversies, and unsolved problems. *Semin Oncol.* 1986;13:434-449. [Bibliographic Links](#) [\[Context Link\]](#)
9. Sarrazin D, Lê MG, Arriagada R, et al. Ten-year results of a randomized trial comparing a conservative treatment to mastectomy in early breast cancer. *Radiother Oncol.* 1989;14:177-184. [\[Context Link\]](#)
10. Fisher B, Redmond C, Poisson R, et al. Eight-year results of a randomized clinical trial comparing total mastectomy and lumpectomy with or without irradiation in the treatment of breast cancer. *N Engl J Med.* 1989;320:822-828. [Bibliographic Links](#) [\[Context Link\]](#)
11. Veronesi U, Banfi A, Salvadori B, et al. Breast conservation is the treatment of choice in small breast cancer: long-term results of a randomized trial. *Eur J Cancer.* 1990;26:668-670. [Bibliographic Links](#) [\[Context Link\]](#)
12. Veronesi U, Salvadori A, Luini A, et al. Conservative treatment of early breast cancer: long-term results of 1232 cases treated with quadrantectomy, axillary dissection, and radiotherapy. *Ann Surg.* 1990;211:250-259. [Bibliographic Links](#) [\[Context Link\]](#)
13. Lichter AS, Lippman ME, Danforth DN, et al. Mastectomy versus breast-conserving therapy in the treatment of stage I and II carcinoma of the breast: a randomized trial at the National Cancer Institute. *J Clin Oncol.* 1992;10:976-983. [Bibliographic Links](#) [\[Context Link\]](#)
14. Blichert-Toft M, Rose C, Andersen JA, et al. Danish randomized trial comparing breast conservation therapy with mastectomy: six years of life-table analysis. *J Natl Cancer Inst Monogr.* 1992;11:19-25. [\[Context Link\]](#)
15. Van Dongen JA, Bartelink H, Fentiman IS, et al. Randomized clinical trial to assess the value of breast-conserving therapy in stage I and II breast cancer, EORTC 10801 trial. *J Natl Cancer Inst Monogr.* 1992;11:15-18. [Bibliographic Links](#) [\[Context Link\]](#)

16. Rand RW, Rand RP, Eggerding F, DenBesten L, King W. Cryolumpectomy for carcinoma of the breast. *Surg Gynecol Obstet.* 1987;165:392-396. [Bibliographic Links](#) [\[Context Link\]](#)
17. Staren ED, Sabel M, Gianakakis LM, et al. Cryosurgery of breast cancer. *Arch Surg.* 1997;132:28-33. [Ovid Full Text](#) [Bibliographic Links](#) [\[Context Link\]](#)
18. Mumtaz H, Hall-Craggs MA, Wotherspoon A, et al. Laser therapy for breast cancer: MR imaging and histopathologic correlation. *Radiology.* 1996;200:651-658. [Bibliographic Links](#) [\[Context Link\]](#)
19. Harari PM, Hynynen KH, Roemer RB, et al. Development of scanned focussed ultrasound hyperthermia: clinical response evaluation. *Int J Radiat Oncol Biol Phys.* 1991;21:831-840. [Bibliographic Links](#) [\[Context Link\]](#)
20. Hill CR, ter Haar GR. High intensity focused ultrasound—potential for cancer treatment. *Br J Radiol.* 1995;68:1296-1303. [Bibliographic Links](#) [\[Context Link\]](#)
21. LeVeen RF. Laser hyperthermia and radiofrequency ablation of hepatic lesions. *Semin Interv Radiol.* 1997;14:313-324. [\[Context Link\]](#)
22. Zlotta AR, Djavan B, Matos C, et al. Percutaneous transperineal radiofrequency ablation of prostate tumour: safety, feasibility and pathological effects on human prostate cancer. *Br J Urol.* 1998;81:265-275. [\[Context Link\]](#)
23. Rosenthal DI, Horniecek FJ, Wolfe MW, Jennings LC, Gebhardt MC, Mankin HJ. Percutaneous radiofrequency coagulation of osteoid osteoma compared with operative treatment. *J Bone Joint Surg Am.* 1998;80:815-821. [\[Context Link\]](#)
24. Zlotta AR, Wildschutz T, Raviv G, et al. Radiofrequency interstitial tumor ablation (RITA) is a possible new modality for treatment of renal cancer: ex vivo and in vivo experience. *J Endourol.* 1997;11:251-258. [Bibliographic Links](#) [\[Context Link\]](#)
25. Powell NB, Riley RW, Troell RJ, Li K, Blumen MB, Guilleminault C. Radiofrequency volumetric tissue reduction of the palate in subjects with sleep-disordered breathing. *Chest.* 1998;113:1163-1174. [Ovid Full Text](#) [Bibliographic Links](#) [\[Context Link\]](#)
26. Wilkinson HA. Percutaneous radiofrequency upper thoracic sympathectomy. *Neurosurgery.* 1996;38:715-725. [Ovid Full Text](#) [Bibliographic Links](#) [\[Context Link\]](#)
27. Baron MS, Vitek JL, Bakay RA, et al. Treatment of advanced Parkinson's disease by posterior GPi pallidotomy: 1-year results of a pilot study. *Ann Neurol.* 1996;40:355-366. [Bibliographic Links](#) [\[Context Link\]](#)
28. Neumann RA, Knobler RM, Pieczkowski F, Gebhart W. Enzyme histochemical analysis of cell viability after argon laser-induced coagulation necrosis of the skin. *J Am Acad Dermatol.* 1991;25:991-998. [Bibliographic Links](#) [\[Context Link\]](#)
29. Gage AA. Cryosurgery in the treatment of cancer. *Surg Gynecol Obstet.* 1992;174:73-92. [Bibliographic Links](#) [\[Context Link\]](#)
30. Rockwell AD. Electro-surgery: benign and malignant tumors. In: Rockwell AD. *The Medical and Surgical Uses of Electricity.* New York, NY: EB Treat & Co; 1903:565-566. [\[Context Link\]](#)
31. Onik GM, Cohen JK, Reyes GD, Rubinsky B, Chang ZH, Baust J. Transrectal ultrasound-guided percutaneous radical cryosurgical ablation of the prostate. *Cancer.* 1993;72:1291-1299. [Bibliographic Links](#) [\[Context Link\]](#)
32. Wong WS, Chinn DO, Chinn M, Chinn J, Tom WL, Tom WL. Cryosurgery as a treatment for prostate carcinoma: results and complications. *Cancer.* 1997;79:963-974. [Bibliographic Links](#) [\[Context Link\]](#)
33. Organ LW. Electrophysiologic principles of radiofrequency lesion making. *Appl Neurophysiol.* 1976/77;39:69-76. [\[Context Link\]](#)
34. Dickson JA, Calderwood SK. Temperature range and selective sensitivity of tumors to hyperthermia: a critical review. *Ann N Y Acad Sci.* 1980;335:180-205. [Bibliographic Links](#) [\[Context Link\]](#)
35. Liu F-F, Wilson BC. Hyperthermia and photodynamic therapy. In: Tannock IF, Hill RP, eds. *The Basic Science of Oncology.* New York, NY: McGraw-Hill Book Co; 1998:443-453. [\[Context Link\]](#)
36. Rhee JG, Song CW. Thermotolerance of organized tissues and tumors. In: Henle KJ, ed. *Thermotolerance.* Vol 1. Boca Raton, Fla: CRC Press Inc; 1987:73-95. [\[Context Link\]](#)
37. Jossinet J. Variability of impedivity in normal and pathological breast tissue. *Med Biol Eng Comput.* 1996;34:346-350. [Bibliographic Links](#) [\[Context Link\]](#)

Accession Number: 00000853-199910000-00006

---



Copyright (c) 2000-2004 [Ovid Technologies, Inc.](#)

Version: rel9.1.0, SourceID 1.9087.1.155