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Preliminary Report of Photodynamic Therapy for Intraperitoneal Sarcomatosis

Todd W. Bauer, MD, Stephen M. Hahn, MD, Francis R. Spitz, MD, Alexander Kachur, PhD, Eli Glatstein, MD, and Douglas L. Fraker, MD

Introduction: Sarcomatosis is the disseminated intraperitoneal spread of sarcoma. It is a condition for which there is no effective treatment. Photodynamic therapy (PDT) is a cancer treatment modality that uses a photosensitizing agent and laser light to kill cells. We report our preliminary Phase II clinical trial experience using PDT for the treatment of intraperitoneal sarcomatosis.

Methods: From May 1997 to December 1998 eleven patients received twelve PDT treatments for intraperitoneal sarcomatosis. Photofrin® (PF) 2.5 mg/kg was administered intravenously 48 hours before surgical debulking to a maximum residual tumor size of less than 5 mm. Light therapy was administered at a fluence of 2.5 J/cm^2 of 532 nm green light to the mesentery and serosa of the small bowel and colon; 5 J/cm^2 of 630 nm red light to the stomach and duodenum; 7.5 J/cm^2 of red light to the surface of the liver, spleen, and diaphragms; and 10 J/cm^2 of red light to the retroperitoneal gutters and pelvis. Light fluence was measured with an on-line light dosimetry system. Response to treatment was evaluated by abdominal CT scan at 3 and 6 months, diagnostic laparoscopy at 3 to 6 months, and clinical examination every 3 months.

Results: Adequate tumor debulking required an omentectomy in eight patients (73%), small bowel resection in seven patients (64%), colon resection in four patients (36%), splenectomy in one patient (9%), and a left spermatic cord resection in one patient. Five patients (45%) have no evidence of disease at follow-up (range, 1.7–17.3 months), including patients at 13.8 and 17.3 months examined by CT. Two patients (18%) died from disease progression. Four patients (36%) are alive with disease progression. Toxicities related to PDT included substantial postoperative fluid shifts with volume overload, transient thrombocytopenia, and elevated liver function tests. One patient suffered a postoperative pulmonary embolism complicated by adult respiratory distress syndrome (ARDS).

Conclusions: Debulking surgery with intraperitoneal PDT for sarcomatosis is feasible. Preliminary response data suggest prolonged relapse-free survival in some patients. Additional follow-up with more patients will be necessary for full evaluation of the added benefit of PDT and aggressive surgical debulking in these patients.

Key Words: Photodynamic therapy—Sarcoma—Photofrin—Laser.

Sarcomatosis is the disseminated intraperitoneal spread of sarcoma. It is associated with a poor prognosis, despite treatments such as repeated debulking and systemic chemotherapy, external beam radiation, and intraperitoneal chemotherapy.[1,2] There is no therapy that results in prolonged disease-free survival. The natural history of these patients is diffuse recurrence of tumor throughout the abdomen with shorter time intervals between symptomatic progression of tumor. In light of the short disease-free interval and high 5-year mortality rate following conventional treatment of intraperitoneal sarcomas, there is a need for more effective treatment for these patients.[1,2]

Photodynamic therapy (PDT) is a treatment modality that combines a photosensitizing agent, laser light of a specific wavelength to activate the sensitizer, and oxygen

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From the Departments of Surgery (TWB, FRS, DLF) and Radiation Oncology (SMH, AK, EG), School of Medicine, University of Pennsylvania, Philadelphia, Pennsylvania.

Dr. Douglas L. Fraker, Chief, Division of Surgical Oncology, Dept. of Surgery, 4 Silverstein, Hospital of the University of Pennsylvania, 3400 Spruce Street, Philadelphia, PA 19104; Fax: 215-662-3629; E-mail: fraker@mail.med.upenn.edu

to kill cells. Hematoporphyrin derivative (HPD) is the first-generation photosensitizing agent most widely used clinically. It is a porphyrin mixture that has been derived from the acid treatment of hematoporphyrin, an organic compound found in hemoglobin. PF (Quadralogic Technologies, Vancouver, British Columbia, Canada) is a partially purified form of HPD. HPD is photochemically activated by the absorption of tissue-penetrating light at 514 nm (green) or 630 nm (red). At these wavelengths, the light and photosensitizer interact with molecular oxygen to produce an excited reactive species (singlet oxygen) which has the capability of killing cells.[3] The quantum yield of singlet oxygen appears to be directly proportional to light absorption and the concentration of tissue oxygen.

The selectivity that makes PDT beneficial as an antineoplastic treatment is the increased retention of PF in tumor compared to normal tissue.[4] Photodynamic therapy has been proposed as treatment for a variety of malignancies and premalignant conditions. Its use has been reported in the treatment of malignancies that include head and neck cancers,[5,6] lung cancer,[7–9] mesothelioma,[10,11] esophageal cancer,[12–15] Barrett's esophagus,[16,17] brain tumors,[18] breast cancer,[19,20] and bladder cancer.[21,22]

The superficial tissue effects of PDT lend themselves to the treatment of surface malignancy, including tumors involving the surface of the peritoneum, such as carcinomatosis and sarcomatosis. Several animal studies have demonstrated the effectiveness of intraperitoneal PDT. Tochner et al.[23] studied PDT in a murine ovarian embryonal carcinoma model. Following two treatments of intraperitoneal HPD and 514 nm light, 6 of 15 mice were cured, whereas all of the control mice died. In another study with four HPD/light treatments they observed a 100% complete response rate and an 85% cure rate.[24]

A Phase I study of debulking surgery and PDT with laser light and PF was conducted by the Surgery and Radiation Oncology Branches of the National Cancer Institute for disseminated intraperitoneal malignancies.[25,26] At follow-up there was an overall cytologic response rate of 76% in evaluable patients, including 3 of the 25 ovarian cancer patients who were disease-free more than 36 months after treatment.[27]

The purpose of this Phase II study is to evaluate the effectiveness of debulking surgery and intraperitoneal PDT using PF and laser light at the maximal intensity defined by the Phase I trial for the treatment of intraperitoneal malignancies. We report our initial results for response to treatment, patient toxicity, and tissue PF levels in patients with sarcomatosis.

MATERIALS AND METHODS

This Phase II trial was approved by the Institutional Review Board and the Clinical Trials Scientific Review and Monitoring Committee of the University of Pennsylvania Cancer Center.

Patient Selection and Evaluation

Patients with overtly disseminated intraperitoneal sarcomas without evidence of hematogenous spread outside of the peritoneal cavity were eligible for entry into this Phase II trial. From May 1997 to December 1998, 11 patients received 12 PDT treatments for intraperitoneal sarcomatosis. Informed consent for participation in the trial was obtained from all patients. Concurrent chemotherapy or radiotherapy was not performed during the PDT treatment period or during the follow-up period unless relapse was documented. The details of previous treatment, histologic diagnosis, and length of disease-free interval prior to PDT are shown in Table 1.

Patients with active extra-abdominal metastatic disease or intrahepatic involvement secondary to metastatic sarcoma were ineligible for the study. Many patients who were seen or who had abdominal CT or MRI scans sent for review were excluded on the basis of unresectability or metastatic disease. Three patients received PF but no PDT because of unresectable disease at laparotomy. Patients with severe liver disease, including cirrhosis, or Grade III-IV elevations in liver function studies, or bilirubin in excess of 1.5 mg/dl were excluded. Other exclusion criteria included regional enteritis, ulcerative colitis, white blood count below 3500/mm^3, platelets less than 100,000/mm^3, serum creatinine above or equal to 2.5 mg/dl, and HIV infection.

Pretreatment evaluation included a complete history and physical examination, complete blood cell count (CBC), electrolytes, bilirubin urea nitrogen (BUN) level, creatinine, glucose, liver function tests, pregnancy test (in women), and electrocardiogram (ECG). Patients also received a chest radiograph and CT scan or MRI of the abdomen and pelvis.

Photofrin Administration

Patients received PF 2.5 mg/kg (reconstituted in either 5% dextrose or 0.9% sodium chloride solution to a final concentration of 2.5 mg/ml) administered intravenously over 15 minutes approximately 48 hours before scheduled laparotomy and PDT treatment. Following PF administration, patients were instructed to avoid direct sunlight for 30 to 60 days because of skin toxicity.

TABLE 1. *Results of treatment received before photodynamic therapy*

Patient no.	Age (y)	Sex	Pathology	Previous surgical debulking	Previous no. surgeries	Prior adjuvant treatment	Disease-free interval from prior surgery to PDT (mo)
1	42	M	Leiomyosarcoma	Small bowel, omentum	2	Chemotherapy	5
2	49	F	Leiomyosarcoma	Small bowel	2		8
3	34	F	Leiomyosarcoma	Tumor only	1		1
4	55	M	Spindle cell	Small bowel, right colon	3	Radiotherapy	2
5	43	M	Leiomyosarcoma	Small bowel	1	Chemotherapy	5
6	57	M	Spindle cell	Unknown	4	Chemotherapy	7
7	45	F	Leiomyosarcoma	Hysterectomy	2	Chemotherapy	4
8	62	M	Spindle cell	Small bowel	1		2
9	41	M	Spindle cell	Spleen	1		3
10	34	F	Synovial cell	Unknown	1	Chemotherapy	22
11	51	F	Leiomyosarcoma	Radical hysterectomy	4	Lupron, IL-2, IFN	16

IL-2, interleukin-2; IFN, interferon.

Surgical Debulking and Photodynamic Therapy

Laparotomy was performed with debulking of all gross tumor to a maximal residual thickness of 5 mm or less. Figure 1 is a preoperative CT scan depicting the extent of intra-abdominal disease in one patient. Figure 2 depicts the surgical specimen from another patient following extensive debulking. The operating room lights were modified with filters (blocking wavelengths below 550 nm) to minimize unwanted activation of the photosensitizer. Six sterile photodiodes (Photop™ UDT-455, Graseby Electronics, Orlando, FL), one mobile and five fixed in the right upper quadrant, left upper quadrant, right paracolic gutter, left paracolic gutter, and midline pelvis anteriorly were used to monitor light dose delivery. The photodiodes permitted real-time fluence rate measurements during the PDT. Laser light was generated using a KTP/532 Laser System (Laserscope, San Jose, CA) and model 630 × P Dye Module (Laserscope). The maximum fluence rate permitted was 150 mW/cm^2.

The optimal wavelength and fluence levels for the various abdominal viscera were worked out in the phase I study. The fluence levels used were the maximum tolerated levels from the phase I trial.[25,26] The bowel and mesentery were treated with a flat-cut tube using 532 nm green light with a tissue penetration of 3 mm. The rest of the abdomen was treated with 630 nm red light with a tissue penetration of 5 mm. Before 630 nm light treatment, the peritoneal cavity was filled with a dilute solution of Intralipid™ (Baxter, Northbrook, IL) (0.01%) in sterile normal saline to minimize shadowing and maximize light diffusion throughout the abdominal cavity and onto all peritoneal surfaces. The wavelength, fluence, and fluence rate of light delivered to the various abdominal viscera are listed in Table 2. Light was delivered to the diaphragmatic surfaces, the liver, the splenic bed, the abdominal wall, the stomach, and the pelvis using an optical fiber sheathed within a modified endotracheal tube (balloon cuff inflated and filled with dilute intralipid). A boost dose of 5–15 J/cm^2 was permitted in patients with gross residual disease. This delivery technique permitted isotropic delivery and prevented thermal burn to the tissues.

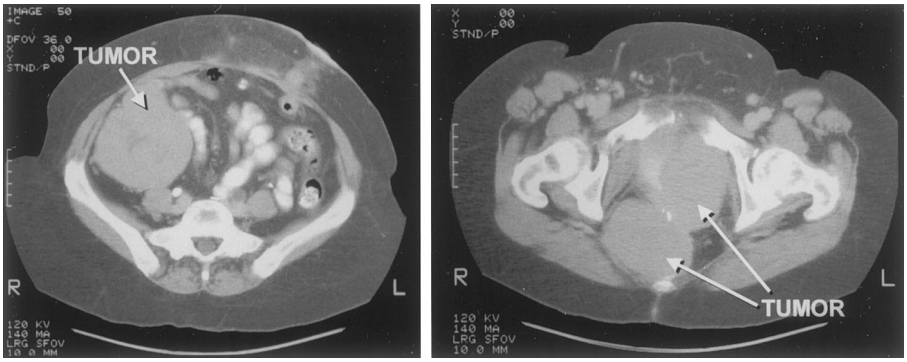

FIG. 1. Preoperative abdominal and pelvic CT scan showing extensive intra-abdominal sarcoma.

FIG. 2. Surgical specimen from a patient following omentectomy, splenectomy, and extensive debulking.

Toxicity Evaluation and Follow-Up

Toxicity was evaluated with the Cooperative Group Common Toxicity Criteria. Patients were seen in the outpatient clinic 1 week after discharge from the hospital and again at 1 month to assess treatment-related toxicities. At that visit the following were performed: history and physical examination, CBC, electrolytes, BUN, creatinine, glucose, liver function tests, and a chest radiograph. This clinical and laboratory evaluation was performed at 1 month after discharge, 3 months after discharge, and then every 3 months thereafter for the first 24 months. A CT scan of the abdomen and pelvis was performed at 3-month intervals. In selected patients a follow-up laparoscopy or laparotomy was performed for restaging.

Response Criteria

Patients with no evidence of abdominal tumor by laparoscopy or diagnostic imaging studies were said to be disease-free. Progressive disease was defined as evidence of new or recurrent intra-abdominal tumor by laparoscopy, diagnostic imaging studies, or peritoneal washings.

TABLE 2. *Intraperitoneal light delivery*

Area treated	Fluence (J/cm^2)	Wavelength (nm)
Mesentery	2.5	532
Small bowel	2.5	532
Large bowel	2.5	532
Diaphragm (R), superior liver	7.5	630
Diaphragm (L), spleen	7.5	630
Anterior stomach	5.0	630
Inferior liver	7.5	630
Omentum, duodenum, posterior stomach	5.0	630
Peritoneal gutter (R)	10.0	630
Peritoneal gutter (L)	10.0	630
Pelvis	10.0	630
Boost to gross disease	5–15.0	630

L, left; R, right.

RESULTS

Eleven patients (6 men and 5 women) were treated with PDT for intraperitoneal sarcomatosis. The mean age was 47 years (range, 34–62). Before entry into this study, five patients (45%) had received chemotherapy, one patient (9%) had received immunotherapy (Lupron, IL-2, and interferon), and one patient had received radiotherapy.

The results of the surgical debulking at the time of PDT are listed in Table 3. All patients had complete resection of all gross tumor or were left with tumor smaller than 5 mm. The light treatment was performed in all patients as per the protocol described in the Materials and Methods section and Table 2. There were no complications during light delivery.

Toxicity data are available for all 11 patients. All patients developed a systemic vascular leak postoperatively and required massive fluid resuscitation. Patients developed generalized edema in the first 1 to 3 days after PDT. Most patients mobilized the fluid within a week after PDT delivery. This toxicity appeared to be worse in patients who required the most extensive debulking. One patient suffered an early postoperative pulmonary embolism further complicated by adult respiratory distress syndrome (ARDS) and volume overload.

Follow-up data are available for all 11 patients. The outcome and current status of these patients are shown in Table 3. The mean length of follow-up is 7.0 months (range, 1.7–17.3). Five patients (45%) have no evidence of disease and are alive at 17.3, 13.8, 5.0, 4.2, and 1.7 months following PDT. Four of these patients have no evidence of disease by abdominal and pelvic CT scan, and two of those four patients have had diagnostic laparoscopy to verify these findings. Six patients (55%) developed intra-abdominal progression of their disease at 8.0, 6.0, 4.0, 2.0, 1.0, and 1.0 months following PDT. Four of these patients are still alive. One patient who developed a recurrence 1 month after PDT died at 5.3 months, and another patient who developed a recurrence at 2 months following PDT died after 4.7 months. One patient who had a recurrence 2 months after initial PDT remained disease-free for 6 months following a repeat PDT. He recently underwent open laparotomy 12 months following his second PDT and was found to have recurrent disease, mostly in his pelvis with minimal disease in his upper abdomen (previously a site of diffuse sarcomatosis).

TABLE 3. *Outcome after PDT for intraperitoneal sarcomatosis (n = 11)*

Patient no.	Debulking at time of PDT	Time to relapse (mo)	Status at last follow-up
1	Omentum, spleen	2	
	Small bowel, sigmoid colon, rectum	8	
	Pelvic tumor[a]		Alive at 11.9 mo
2	Omentum	NED	Alive at 17.3 mo
3	Omentum, small bowel	NED	Alive at 13.8 mo
4	Small bowel, right colon, transverse colon	1	Dead at 5.3 mo
5	Omentum, small bowel, appendix, rectum, left spermatic cord	4	Alive at 4.4 mo
6	Small bowel	6	Alive at 6.0 mo
7	Omentum, small bowel, left colon	2	Dead at 4.7 mo
8	Omentum, small bowel	NED	Alive at 4.2 mo
9	Omentum	NED	Alive at 5.0 mo
10	Tumor only	1	Alive at 3.2 mo
11	Omentum, small bowel	NED	Alive at 1.7 mo

[a] Surgery only—no PDT.
NED, no evidence of disease; PDT, photodynamic therapy. References.

DISCUSSION

The best chance of curing patients with abdominal and retroperitoneal sarcoma is with complete resection at initial operation. However, the outcome following conventional treatment for gastrointestinal soft tissue (GIST) and retroperitoneal sarcoma has been disappointing, even for patients with localized, completely resectable disease. Recurrence rates for published series are between 25% and 82%.[1,2,28,29] Heslin et al.[30] reported a 5% per year recurrence rate in 198 adult patients following resection of retroperitoneal sarcoma. The distinction between GIST and retroperitoneal sarcomas at initial presentation is important due to the different behaviors of the two tumor types. Once the disease progresses to diffuse intraperitoneal involvement, or sarcomatosis, as in all of the patients entered into this study, this distinction becomes much less significant.

Even when patients do not develop bloodborne metastases, the diffuse nature of the tumor recurrence throughout the abdomen limits the capability and benefit of further debulking surgery. An additional treatment that could be delivered to all peritoneal surfaces with acceptable toxicity would be a significant benefit if it were effective in destroying tumor. PDT theoretically treats all peritoneal surfaces. In a preclinical model using a human sarcoma xenograft, PDT with PF is effective against sarcoma.[31]

Prior clinical studies have evaluated PDT in the peritoneum as a focal adjuvant treatment for sarcoma and for diffuse peritoneal disease of multiple histologies. Nambisan et al.[32] evaluated complete surgical resection plus PDT to the tumor bed in 10 patients with localized retroperitoneal sarcoma. Twenty percent of patients had no evidence of disease more than 2 years after treatment, including one patient at 28 months and another patient at 24 months. Sindelar et al.[27] at the NCI reported the results of a Phase I study with escalating light energy levels evaluating debulking surgery and PDT for disseminated intraperitoneal malignancies. In the 12 patients with sarcomatosis, the median relapse-free interval was 7 months (range, 2–55), one patient was alive with no evidence of disease at more than 24 months, and another patient was alive with no evidence of disease at more than 36 months. Only two patients on that initial Phase I trial with sarcomatosis were treated at the highest dose level, and both patients had bulky disease with early recurrence after PDT.

The initial results of this Phase II study have demonstrated that debulking surgery to the required tumor size and PDT is feasible in patients with intraperitoneal sarcomatosis. There were treatment-related toxicities, all of which were reversible. The most notable and significant toxicity is fluid sequestration requiring massive fluid resuscitation, with significant whole-body edema maximal at 1 to 3 days after treatment. Five (45%) of the 11 patients have no evidence of disease as of last follow-up. Notably, two patients are disease-free at more than 1 year following PDT, including patients who had developed recurrences at 1 month and 8 months before receiving PDT. Three additional patients (27%) are disease-free at 1.7 to 5 months. One patient whose disease-free interval was 2 months before PDT is now disease-free 4.2 months following PDT. A second patient whose disease-free interval was 3 months before PDT is now disease-free 5 months following PDT. These results have been achieved with debulking surgery and a single application of PDT; no additional postoperative adjuvant were treatments given.

Our plan is to continue follow-up on these patients and to treat additional patients. The success of PDT depends on the ability to kill every tumor cell in the abdomen. We are working with the physicists to further optimize light delivery, and we plan to evaluate newer second-generation photosensitizers, which may have greater tumor specificity.

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REFERENCES

1. Storm FK, Eilber FR, Mirra J, Morton DL. Retroperitoneal sarcomas: reappraisal of treatment. *J Surg Oncol* 1981;17:1–7.
2. Kinsella TJ, Sindelar WF, Lack E, Glatstein E, Rosenberg SA. Preliminary results of a randomized study of adjuvant radiation therapy in resectable retroperitoneal soft tissue sarcomas. *J Clin Oncol* 1988;6:18–25.
3. Foote CS. Mechanisms of photooxygenation. *Prog Clin Biol Res* 1984;170:3–18.
4. Gomer CJ, Dougherty TJ. Determination of [3H]- and [14C]hematoporphyrin derivative distribution in malignant and normal tissue. *Cancer Res* 1979;39:146–51.
5. Biel MA. Photodynamic therapy and the treatment of head and neck cancers. *J Clin Laser Med Surg* 1996;14:239–44.
6. Grant WE, Speight PM, Hopper C, et al. Photodynamic therapy: an effective, but non-selective treatment for superficial cancers of the oral cavity. *Int J Cancer* 1997;71:937–42.
7. Cortese DA, Edell ES, Kinsey JH. Photodynamic therapy for early stage squamous cell carcinoma of the lung. *Mayo Clin Proc* 1997;72:595–602.
8. Kato H, Okunaka T, Shimatani H. Photodynamic therapy for early stage bronchogenic carcinoma. *J Clin Laser Med Surg* 1996;14: 235–8.
9. McCaughan JS, Williams TE. Photodynamic therapy for endobronchial malignant disease: a prospective fourteen-year study. *J Thorac Cardiovasc Surg* 1997;114:940–7.
10. Mostal TL, Dougherty TJ, Urschel JD, et al. Operation and photodynamic therapy for pleural mesothelioma: 6-year follow-up. *Ann Thorac Surg* 1998;66:1128–33.
11. Pass HI, Delaney T, Tochner Z, et al. Intrapleural photodynamic therapy. *Ann Surg Onc* 1996;1:28–37.
12. Lightdale CJ, Heier SK, Marcon NE, et al. Photodynamic therapy with porfimer sodium versus thermal ablation with Nd:YAG laser for palliation of esophageal cancer: a multicenter randomized trial. *Gastrointest Endosc* 1995;42:507–12.
13. McCaughan JSJ, Nims TA, Guy JT, Hicks WJ, Williams TEJ, Laufman LR. Photodynamic therapy for esophageal tumors. *Arch Surg* 1989;124:74–80.
14. Likier HM, Levine JG, Lightdale CJ. Photodynamic therapy for completely obstructing esophageal carcinoma. *Gastrointest Endosc* 1991;37:75–8.
15. Marcon NE. Photodynamic therapy and cancer of the esophagus. *Semin Oncol* 1994;21:20–3.
16. Overholt BF, Panjehpour M. Barrett's esophagus: photodynamic therapy for ablation of dysplasia, reduction of specialized mucosa, and treatment of superficial esophageal cancer. *Gastrointest Endosc* 1995;42:64–70.
17. Laukka M, Wang K. Initial results using low-dose photodynamic therapy in the treatment of Barrett's esophagus. *Gastrointest Endosc* 1995;42:59–63.
18. Muller PJ, Wilson BC. Photodynamic therapy of malignant primary brain tumours: clinical effects, post-operative ICP, and light penetration of the brain. *Photochem Photobiol* 1987;46:929–35.
19. Sperduto PW, DeLaney TF, Thomas G, et al. Photodynamic therapy for chest wall recurrence in breast cancer. *Int J Radiat Oncol Biol Phys* 1991;21:441–6.
20. Schuh M, Nseyo UO, Potter WR. Photodynamic therapy for palliation of locally recurrent breast carcinoma. *J Clin Oncol* 1987; 5:1766–70.
21. Benson RC. Treatment of diffuse transitional cell carcinoma in situ by whole bladder hematoporphyrin derivative photodynamic therapy. *J Urol* 1985;134:675–8.
22. Harty JI, Amin M, Wieman TJ, Tseng MT, Ackerman D, Broghamer W. Complications of whole bladder dihematoporphyrin ether photodynamic therapy. *J Urol* 1989;141:1341–6.
23. Tochner Z, Mitchell JB, Harrington FS, Smith P, Russo DT, Russo A. Treatment of murine intraperitoneal ovarian ascitic tumor with hematoporphyrin derivative and laser light. *Cancer Res* 1985;45: 2983–7.
24. Tochner Z, Mitchell JB, Smith P, Harrington F, Glatstein E, Russo D, Russo A. Photodynamic therapy of ascites tumours within the peritoneal cavity. *Br J Cancer* 1986;53:733–6.
25. Sindelar WF, DeLaney TF, Tochner Z, et al. Technique of photodynamic therapy for disseminated intraperitoneal malignant neoplasms. Phase I study. *Arch Surg* 1991;126:318–24.
26. DeLaney TF, Sindelar WF, Tochner Z, et al. Phase I study of debulking surgery and photodynamic therapy for disseminated intraperitoneal tumors. *Int J Radiat Oncol Biol Phys* 1993;25:445–57.
27. Sindelar WF, Sullivan FJ, Abraham E, et al. Intraperitoneal photodynamic therapy shows efficacy in phase I trial. *Proc Am Soc Clin Oncol* 1995;14:447. Abstract 1550.
28. Kilkenny JW 3rd, Bland KI, Copeland EM 3rd. Retroperitoneal sarcoma: the University of Florida experience. *J Am Coll Surgeons* 1996;182:329–39.
29. Karakousis C, Gerstenbluth R, Kontzoglou K, Driscoll DL. Retroperitoneal sarcomas and their management. *Arch Surg* 1995;130: 1104–9.
30. Heslin M, Lewis J, Nadler E, et al. Prognostic factors associated with long-term survival for retroperitoneal sarcoma: implications for management. *J Clin Oncol* 1997;15:2832–9.
31. Engbrecht BW, Menon C, Kachur AV, Hahn SM, Fraker DL. Photofrin-mediated photodynamic therapy induces vascular occlusion and apoptosis in a human sarcoma xenograft model. *Cancer Res* 1999;59:4334–42.
32. Nambisan RN, Karakousis CP, Holyoke ED, Dougherty TJ. Intraoperative photodynamic therapy for retroperitoneal sarcomas. *Cancer* 1988;61:1248–52.