Photodynamic therapy (PDT) is an antitumor method that uses a nontoxic photosensitizer and visible light to produce cytotoxic reactive oxygen species (ROS) that destroy malignant cells. It has been increasingly used in the treatment of non-melanoma skin cancers, particularly basal cell carcinoma (BCC), providing a high degree of tumor regression and excellent aesthetic results. We report the case of a patient with histopathologically proven superficial BCC in which regression of untreated contiguous tumor was noted after PDT.

**Case Report**

PDT was administered to a 60-year-old woman with histopathologically proven superficial BCC near the nasal tip. Informed consent was obtained from the patient according to the approved protocol of the institutional ethics committee, which was in agreement with the guidelines of the 1975 Declaration of Helsinki. The patient reported no prior personal history of skin cancer and subsequently consented to PDT at the Plastic Surgery Unit of the Hospital Oncology Service, Instituto Venezolano de los Seguros Sociales. The physician observed the vital signs of the patient as well as the response of the tumor to the treatment during the first minutes; at 6, 24, and 48 hours; at the first week; weekly for 8 weeks; and every 3 months for 1 year.

The photosensitizer used in this treatment was the commercial chlorin derivative Photolon (Chlorine e6-PVP, Scientific Pharmaceutical Center, RUE Belmedpreparaty, Minsk, Belarus). The drug dose was 1.7 mg/kg of body weight diluted in 200 mL of saline solution injected intravenously slowly over a 20-minute period; the drug–light application interval was 3 hours. The light source used was the diode laser (ML-662-SP, Milon Laser Ltd., Sain-Peterburg, Russia) with 662-nm wavelength and 2.5-W optical power, and the light dose was 100 J/cm², delivered at a fluency rate of 170 mW/cm² with a 12-mm spot size, which covered only the detected lesion. The patient was kept in the dark from the application of the photosensitizer until she left the hospital unit, during the night. No serious side effects or complications during or after treatment were observed other than transient mild local pain and moderate edema followed by a crusted ulcer formation after 1 week.

Figure 1 shows the 10-mm tumor zone before PDT, including the area on the left of the photo-
Figure 1. Photograph showing the 10-mm basal cell carcinoma near the nasal tip before photodynamic therapy.

Figure 2. Seven days after photodynamic therapy, photograph showing crusted ulcer formation in a 10-mm treated tumor and in a contiguous untreated zone.

Figure 3. Spot laser illumination over the treated tumor area during photodynamic therapy.

Figure 4. Eighty days after photodynamic therapy. Healing of the tumor with epithelialization and acceptable aesthetic results.

discussion
Selective accumulation of chlorine e6-PVP in tumor cells has already been demonstrated, and this is the basis for selective PDT and diagnosis. Moreover, according to this report, the e6-PVP induced cell death via apoptosis and also via necrosis. Photosensitizers are known to induce cell killing through type I reactions in which electron transfer occurs between the light-excited photosensitizer and cellular constituents or type II reactions that involve energy transfer between the excited photosensitizer and molecular oxygen to produce singlet oxygen. For Photolon, it has been demonstrated that the mechanism of induced cell death involves the induction of ROS through a type I mechanism.
During oxidation, proteins can lose amino acids or can be fragmented. Those reactions lead to alteration of structural proteins or alteration of enzyme functions. Overall increases in the relative level of organic hydroxyl, carbonyl, and carboxyl-free radical groups (alkoxyl radical RO,
½ half-life 1 μs, peroxyl radical ROO• half-life 7 seconds, and hydroperoxyl radical ROOH•), generating a diffusible effect that can extend to nearby tissue, accompany protein and amino acid oxidation. Free radicals produced by type II reactions have a half-life that lasts from 1 ns to 10 μs (superoxide ion O2•− 10 μs, singlet oxygen 1O2 1 μs, and hydroxyl radical OH• 1 ns). This is in agreement with the report of deeper and more-extensive necrosis in patients treated with Photolon than in those treated with Radachlorin and Photoditazine1 which may be acting through a type II reaction.

The findings of this study suggest that the necrosis and regression of the untreated tumor area shown in Figure 2 may be related to the ROS generated at the irradiated tumor site. It may be that the diffusion of these cytotoxic agents from the irradiated zone to the neighborhood tumor zone causes the simultaneous development of the necrosis also on this untreated zone. This is in agreement with the fact that BCC has greater microvessel density than surrounding normal tissue. 2

In summary, PDT with Photolon is an effective method for the treatment of BCC that provides acceptable functional and aesthetic results without major adverse effects. We hypothesize that, in addition to its direct effect on BCC tumor cells, Photolon-PDT generates diffusible and relatively stable ROS so as to produce regression of contiguous untreated tumors.

References

Address correspondence and reprint requests to: Humberto Cabrera, PhD, Instituto Venezolano de Investigaciones Científicas, Carretera a Jají, Km 29, Mérida 5101, Venezuela, or e-mail: hcabrera@ivic.gob.ve; cabrera_25@yahoo.com