Using feedback for cancer treatment

Stefan Andersson-Engels and Johan Axelsson

Advances in monitoring the response to photodynamic therapy may permit real-time dosage adjustments, improving the outcome for patients.

In 2006, there were an estimated 345,000 cases of prostate cancer in Europe. The resulting 87,000 deaths\(^1\) demonstrate the need for improvements in treatment to minimize side effects and enable therapy of tumors that have already received a full quota of ionizing radiation. Several minimally invasive therapies are already under development and evaluation, including interstitial photodynamic therapy (PDT), which shows promise as a treatment for large internal malignant tumors.

Photodynamic therapy has long been successfully implemented as a treatment for conditions such as age-related macula degeneration and non-melanoma skin cancer. The technique is attractive because it induces only limited damage to DNA and connective tissue structures and is therefore not considered cancerogenic. It could play an important role in the management of tumors that recur after treatments such as radiotherapy or surgery, which often cannot be repeated. PDT requires the simultaneous presence of light, photosensitizer, and oxygen and has the advantage of being truly local. A doctor can use appropriate light delivery systems to tailor the light distribution to the target tissue. For these reasons, PDT could become a very valuable treatment for recurrent prostate cancer.\(^2,3\)

The main challenge when using PDT to treat a bulk prostate cancer tumor is to reach the entire tumor. Limited penetration of light means that in order to distribute the light as evenly as possible over the tumor volume, the light has to be delivered interstitially with a few long cylindrical diffusers or many point-emitting optical fibers. In our research we have opted to use the latter approach, which also provides a valuable opportunity to use the fibers to monitor the treatment effect. Other organs close to the prostate (such as sphincters controlling urinary flow, nerves and the rectum) are vulnerable to damage, and so this spectroscopic guidance is particularly important. These critical tissue structures make it necessary to control the treatment dose much more accurately than in other, more conventional, PDT applications.

Treatment parameters alter as the PDT is administered and this brings out the importance of individualized intraoperative monitoring to delivering the optimum dose. Unfortunately, treatment response only becomes obvious after a few days and cannot be measured directly. To overcome this, we used the

Figure 1. Spatially- (left) and temporally-resolved (right) measurements of optical properties. In the spatially resolved schematic, a source in the middle delivers the light and the surrounding fibers collect the light at different source-detector distances. The diagram (lower left) shows the intensity as a function of distance. In the temporally resolved schematic, three photon paths are shown, short (red), moderate (blue), and long (green). The diagram (lower right) shows the intensity as a function of time where the timing of each photon path is indicated with a color-coded arrow.

Continued on next page
‘explicit PDT dosimetry’ model for relating proxy parameters such as the amount of light, photosensitizer, and oxygen in the treatment volume to outcome. We were able to spatially map these parameters because we had used multiple fibers to deliver the light.

Here we present maps of these parameters from a patient in a clinical PDT multicenter study conducted by SpectraCure AB. The patient received the photosensitizer Foscan® 96 hours prior to the treatment. The treatment procedure has been described elsewhere. We assessed the light fluence rate distribution by assessing the optical properties from spatially or temporally resolved measurements, as shown in Figure 1.

We subsequently modeled the light propagation and calculated the light fluence rate throughout the entire prostate and surrounding tissue by using regional values for the optical properties around each fiber. The fluence rate in one plane through a prostate is illustrated in Figure 2a. In addition, the high number—eighteen—of optical fibers used in this treatment made it possible to reconstruct tomographically the photosensitizer concentration from the fluorescence measurements. This is illustrated in Figure 2b.

After considering the results of interoperative measurements, we adjusted the total light treatment dose by varying the light delivery time. A schematic of the treatment dosimetry module is depicted in Figure 3.

We have shown how clinical photodynamic therapy of prostate cancer can be monitored during treatment in order to deliver the most appropriate dose. This is an important step in optimizing and predicting the treatment outcome. Currently we are in an early stage of a phase I-II clinical study. If it is successful, interstitial photodynamic therapy with real-time treatment control could well become an important alternative to current treatment options.