

The research presented in this thesis emanates from six separate clinical research projects investigating the *in vivo* measurement of light and the role of tissue optical properties in oncological applications of light. While the primary objectives of each of the individual projects were very diverse, the research presented here has a common thread centred on the *in vivo* measurement of light. The distribution of light within tissue is of vital importance in photodynamic therapy and is strongly dependent on the *in vivo* optical properties of tissue. Differences and variations in tissue optical properties are also of vital importance for optical diagnostics.

This thesis investigates the *in vivo* spatial and temporal variations in tissue optical properties and their importance for optical diagnostics and monitoring of therapy. We have developed dedicated light delivery and measurement devices, and performed clinical *in vivo* measurements during PDT, and during surgical and biopsy guided optical diagnostic procedures. The first sections of this thesis (chapters 2 – 5) concerns the role of intra- and inter-patient variations of tissue optical properties, their temporal behaviour, and the importance of *in vivo* light measurements in PDT. The second section (Chapters 6 – 10) describes the measurement of *in vivo* tissue optical properties and their relationship to optical diagnostics.

We draw the following general conclusions from the research on *in vivo* light measurements presented in this thesis:

- I. Optical properties vary between patients and in healthy subjects for similar tissue types.
- II. Optical properties are distributed inhomogeneously within the treatment or diagnostic volume of interest.
- III. Optical properties have shown to change during PDT.
- IV. *In vivo* variations in tissue optical properties and in particular the absorption properties are primarily related to the total amount of blood and its oxygenation in region of interest.

Considering these four general conclusions with respect to their consequences for PDT and optical diagnosis, the following specific conclusions are drawn:

With respect to PDT:

- Light delivery based on a fixed source output power and surface area or volume could lead to clinically unacceptable complications and insufficient tumour response.
- Predefined light delivery planning based on the assumption that *in vivo* optical properties are static and homogeneously distributed within the treatment volume could lead to clinically unacceptable complications and insufficient tumour response.
- We postulate that performing light dosimetry during PDT basing the administered fluence (rate) on what is measured *in situ*, may significantly improve clinical response and reduce the incidence of complications.
- The concept of *in situ* based dosimetry should be taken in consideration for any specific application of PDT, especially for applications that involves cavity illuminations, e.g. bladder and the Barrett's oesophagus.

And with respect to optical diagnostics,

- Diffuse reflectance methods that employ the use of multiple wavelengths should take into account that for each of these wavelengths a different tissue volume is sampled as a result of tissue mediated differences in path length of the detected photons.
- Optical diagnostic methods that employ the use of multiple detection fibres at different source detector fibre distances should consider that for the same wavelength a

different tissue volume is sampled.

- Diffuse reflectance models that assume a homogeneous distribution of optical properties used for the analysis of reflectance data harvested from a heterogeneous media, results in unstable modelling consequently, thus generating unreliable optical properties.
- The inhomogeneous distribution of haemoglobin concentrated in discrete cylindrical vessels can be corrected for. This correction is in our opinion of vital importance for the analysis of any future methods that employ diffuse reflectance data below 650nm.
- For functional optical diagnosis, the average optical properties of malignant tissue structures should dominate the average optical properties of the surrounding heterogeneous normal tissue.

In conclusion, the findings presented here should be taken into consideration when developing new optical diagnostic tools, theoretical models of light distribution, light delivery and dosimetry planning for PDT.