

Z-scan technique: A new concept for Diagnosis of Prostate Cancer in blood

Camila T. Nabeshima^a, Sarah Isabel Pinto Alves^a, Antonio Martins F. Neto^b, Flávia R. O. Silva^c,
Ricardo Elgul Samad^c, Lilia C. Courrol^a

^aUniversidade Federal de São Paulo (UNIFESP), Laboratório de Lasers e Óptica Biomédica Aplicada, Instituto de Ciências Ambientais Químicas e Farmacêuticas (ICAQF), Departamento de Ciências Exatas e da Terra, Diadema, Brazil

^bUniversidade de São Paulo (USP), Instituto de Física, São Paulo, SP, Brazil

^cCentro de Lasers e Aplicações, IPEN-CNEN/S, São Paulo, SP, Brazil

[*lccourrol@gmail.com](mailto:lccourrol@gmail.com)

Abstract: Porphyrin accumulate substantially more in tumors than in normal tissues. The optical nonlinearity of the blood porphyrin was analyzed using Z-scan technique. The results showed a decrease in nonlinear refractive index value for tumor blood.

OCIS codes: 190.1900 Nonlinear optics; 300.6420 Spectroscopy, nonlinear 300.0300 Spectroscopy; 170.6280 Spectroscopy, fluorescence and luminescence

1. Introduction

Prostate cancer is the most common non-skin related male cancer type in the world. Prostate cancer is diagnosed using a variety of tests including biopsies of the prostate, digital rectal examination, transrectal ultrasonography, and assaying prostate-specific antigen (PSA)[1]. Excluding biopsies, these methods are widely employed, but are very limited in their ability to diagnose prostate cancer since they cannot distinguish between benign enlargements of the prostate, prostate inflammation and a cancerous prostate[2].

Here we report the measurement of the nonlinear refractive index of blood porphyrin[3] by the Z-scan to determine if this technique can be used as a complementary tool to diagnose the prostate cancer.

Experimental Setup

A total of 6 male NUDE mice, ~8 weeks old on arrival were divided into 2 groups: Control, and Tumor (inoculation with DU145 cells). The animals had their blood collected, 39 after inoculation and protoporphyrin IX extraction [3] was performed.

Protoporphyrin Standard (Sigma Porphyrin. Products, Logan, Utah, USA) was dissolved in acetone (analytical purity) and solutions containing concentrations of 0.01, 0.05, 0.1, 0.2, 0.4, 0.6, 0.8, 1.5 and 3.0 µg/mL were prepared in triplicate. Z-Scan set-up was composed by a continuous-wave (CW) Nd:YVO₄ (λ=532 nm) laser model Verdi V10 from Coherent, with a Gaussian profile beam. In this set-up the laser beam was chopped at 17 Hz and focused by a lens with focal distance f=90 mm. Transmitted light was collected by a silicon photo detector, positioned at the far field. The power of the beam was set to obtain the Z-Scan peak-to-valley dependence curve in the limit of the technique, i.e., the normalized transmittance lies between 1.2 and 0.8. All measurements were performed in a quartz cell with 1mm path length.

3. Results and Conclusions

In this study, initially, a calibration curve was determined from porphyrin solutions; then, blood from normal Nude male mice and blood from Nude male mice in which prostate cancer was induced by DU145 cells intraprostatic inoculation had their optical nonlinearities measured, and compared to the calibration curve.

The average Z-Scan results of the blood extracted from three healthy and three cancerous animals are shown in Figure 1.

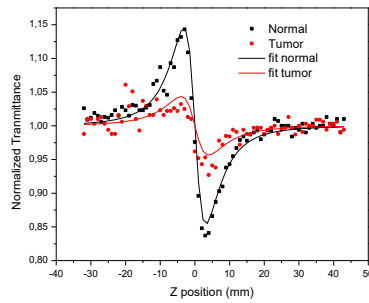


Figure 1: Z-scan data for the animal blood. Each curve corresponds to the average normalized transmittance of 3 animals, before and 39 days after inoculation.

We have measured the nonlinear refractive index (n_2) of protoporphyrin IX acetone solutions with concentrations varying from 0 to 0.3 $\mu\text{g/mL}$, and from blood samples of normal and prostate tumor induced animal by employing the Z-scan technique with a 532 nm Nd:YAG CW laser, data are shown in the table 1. The Z-scan measurements indicate that standard protoporphyrin IX samples and blood samples exhibit opposite nonlinear optical behaviors. This difference could be obtained due to the changes in pH of extracellular matrix in blood of animal with tumor.

Table 1: The nonlinear refractive index (n_2) of protoporphyrin IX acetone solutions with concentrations varying from 0 to 0.3 $\mu\text{g/mL}$, and from blood samples of normal and prostate tumor induced animal by employing the Z-scan technique.

| PPIX [$\mu\text{g/mL}$] | ϕ (rad) | α (cm^{-1}) | L_{ef} (cm) | n_2 (cm^2/W) |
|---------------------------|--------------|-------------------------------|----------------------|----------------------------------|
| 0.3 | -0.62424 | 0.017 | 0.099915048 | -5.85124E-09 |
| 0.15 | -0.29720 | 0.0089 | 0.099955513 | -2.78464E-09 |
| 0.08 | -0.14594 | 0.0102 | 0.099949017 | -1.36749E-09 |
| 0.06 | -0.07603 | 0.0102 | 0.099949017 | -7.12416E-10 |
| 0.02 | -0.04344 | 0.0102 | 0.099949017 | -4.07041E-10 |
| 0.01 | -0.05713 | 0.0102 | 0.099949017 | -5.35319E-10 |
| 0.005 | -0.05345 | 0.0069 | 0.099965508 | -5.00754E-10 |
| 0.001 | -0.20524 | 0.0056 | 0.099972005 | -1.9227E-09 |
| 0 | -0.03812 | -8.57E-04 | 0.100004283 | -3.56994E-10 |

| Sample | ϕ (rad) | n_2 (cm^2/W) |
|--------|--------------|----------------------------------|
| normal | -0,72246 | -6.7719E-09 |
| 39d | -0.21458 | -2.0113E-09 |

Acknowledgements

Fapesp 2014/069609 for financial support.

4. References

1. A. Morlacco, J. Pan, and R. J. Karnes, "Risk-prediction tools in prostate cancer: the challenge of tailoring," Asian J Androl (2016).
2. S. La Vignera, R. A. Condorelli, G. I. Russo, G. Morgia, and A. E. Calogero, "Endocrine control of benign prostatic hyperplasia," Andrology 4, 404-411 (2016).
3. F. R. de Oliveira Silva, M. Helena Bellini, V. Regina Tristao, N. Schor, N. D. Vieira, Jr., and L. C. Courrol, "Intrinsic Fluorescence of Protoporphyrin IX from Blood Samples Can Yield Information on the Growth of Prostate Tumours," Journal of Fluorescence 20, 1159-1165 (2010).