

Early Detection and Treatment Monitoring of Human Breast Cancer MCF-7 Using Fluorescence Imaging



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Introduction

- Early detection and treatment is the best solution to increasing the survival rate of breast cancer patients. If tumor cells are detected before spreading, therapies are less invasive and more effective in eradicating the cancer.
- Human estrogen-dependent breast cancer cell line MCF-7 has been used in many studies to test new drug and therapy efficiency.
- Treatment of xenograft tumors is usually started when mice develop palpable tumors.
- Fluorescence imaging has been widely applied in small animal models⁽¹⁾.
- We hypothesize that fluorescence imaging of MCF-7 tumor expressing green fluorescence protein (GFP) may serve as a tool to detect non-palpable tumor growth and monitor its treatment early.
- Here we present here results on the early detection of human breast cancer MCF-7 as well as monitoring its treatment in nude mice using a time-domain *in vivo* small animal fluorescent molecular imaging system.

Materials and Method

Cells and Mouse Model

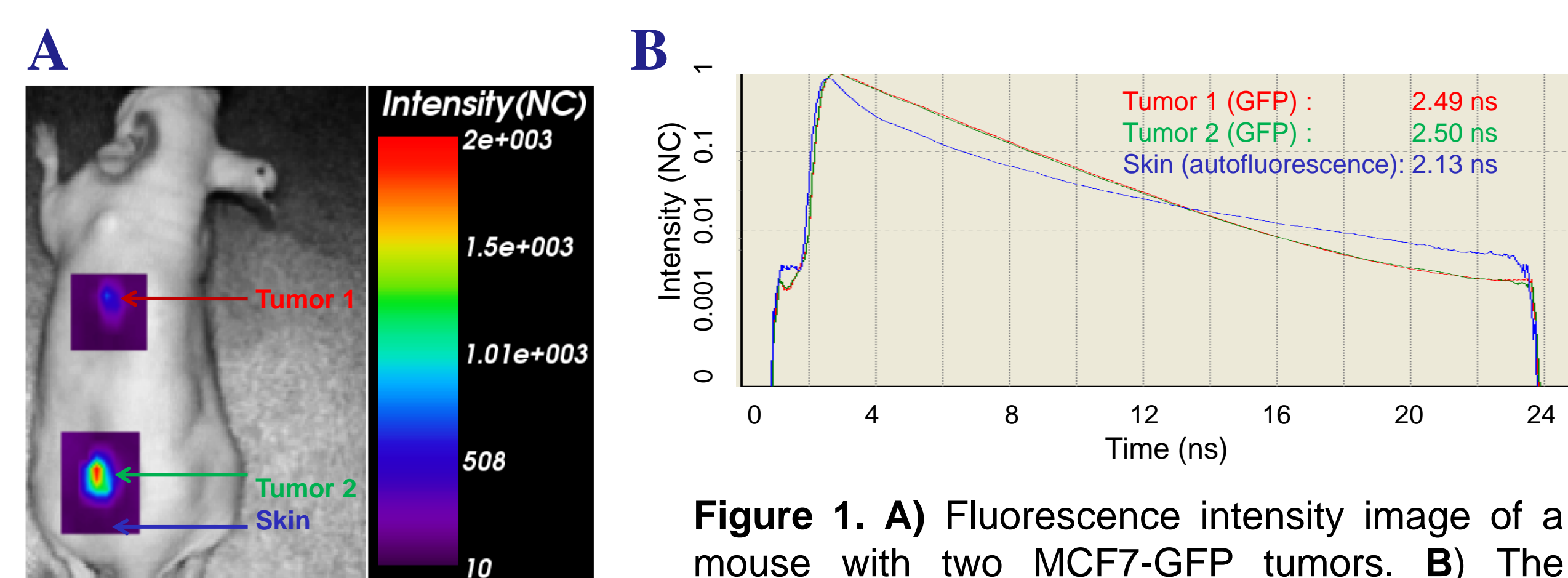
- Human breast cancer MCF-7 cell line expressing GFP was cultured in DMEM + 10% FBS + G418 in standard condition, and harvested in PBS/Matrigel (1:1) for mice injection.
- CD-1 nude female adult mice aged 6-8 weeks received subcutaneous injections of 2 million cells. 17- β -estradiol (0.72mg, 60 days release) and tamoxifen (5mg, 60 days release) pellets (Innovative Research of America, USA) were implanted 2 weeks before, and 2 weeks post-injection of cancer cells, respectively.
- Mice were euthanized, and tumors were excised for *ex vivo* tumor imaging. All procedures were in accordance with the Canadian Council on Animal Care.

Fluorescence Molecular Lifetime Imaging

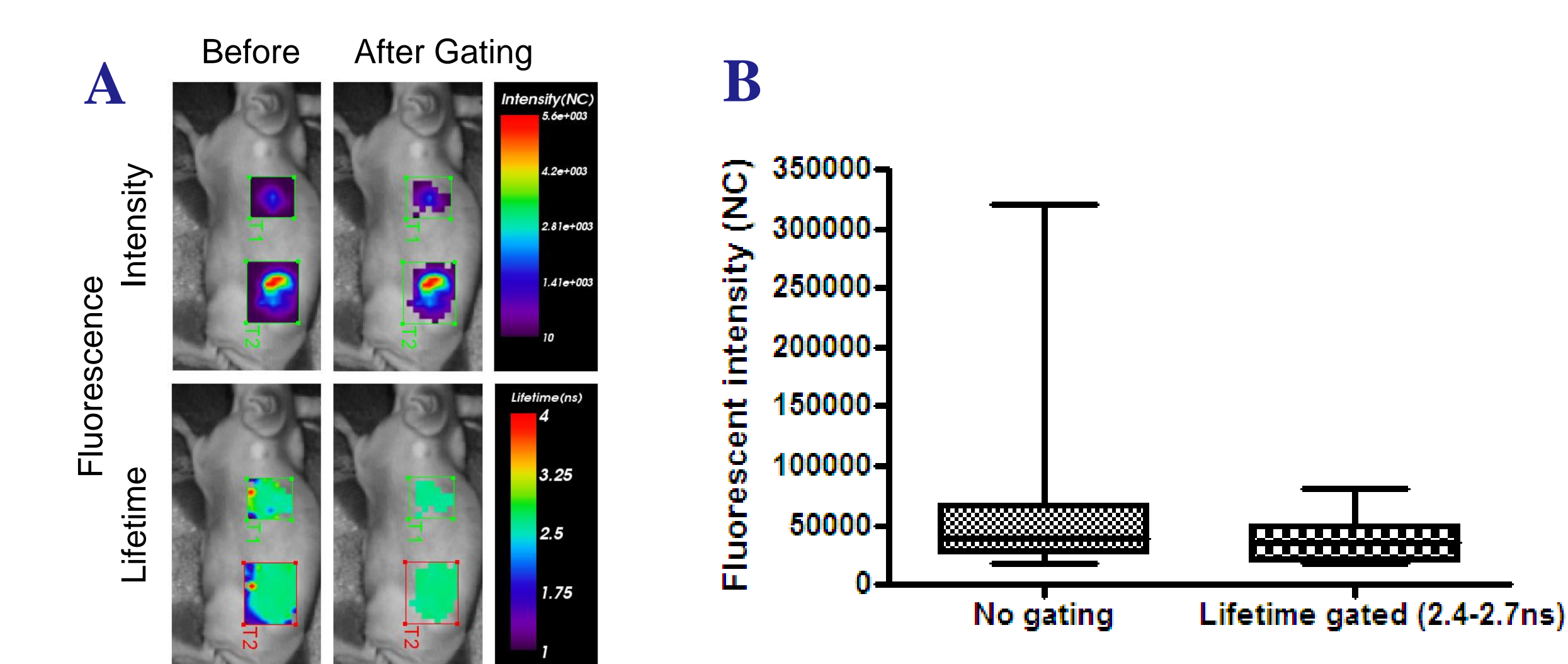
- Fluorescence imaging was performed with the highly sensitive fluorescence lifetime imager Optix MX2⁽²⁾. Mice were maintained with isoflurane anesthesia throughout every *in vivo* imaging study conducted.
- All acquired data was processed using the OptiView™ analysis software. GFP expression *in vivo* was determined by measurement of fluorescence intensity, lifetime and location of the tumors over the time and confirmed by *ex vivo* tumor imaging. Statistical analyses were performed with Prism4.

Results

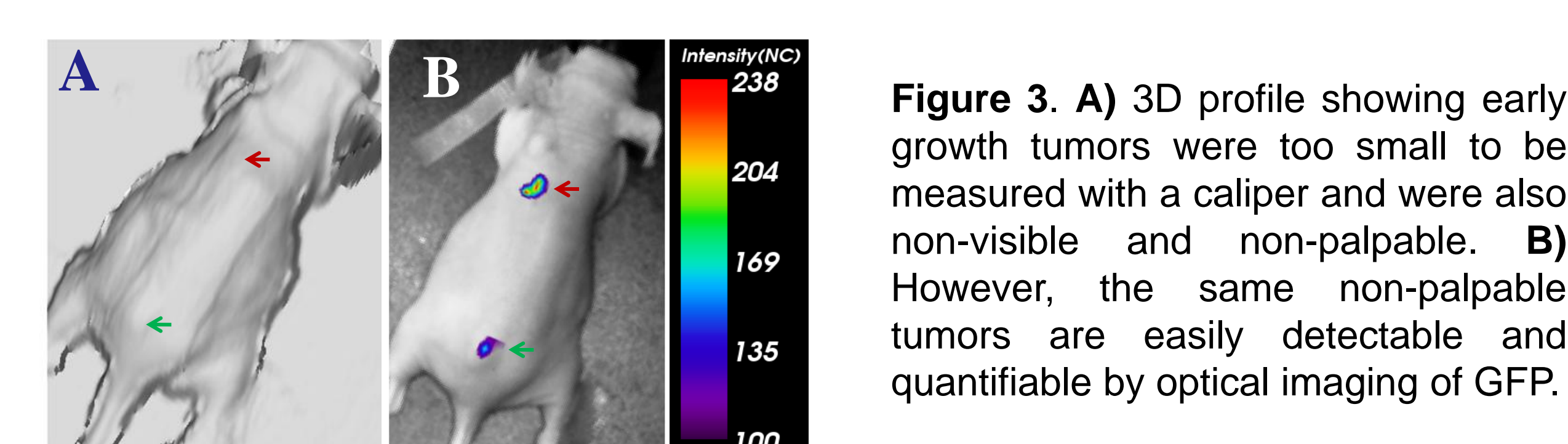
1. Distinguishing GFP Signal from Autofluorescence Utilizing Fluorescence Lifetime



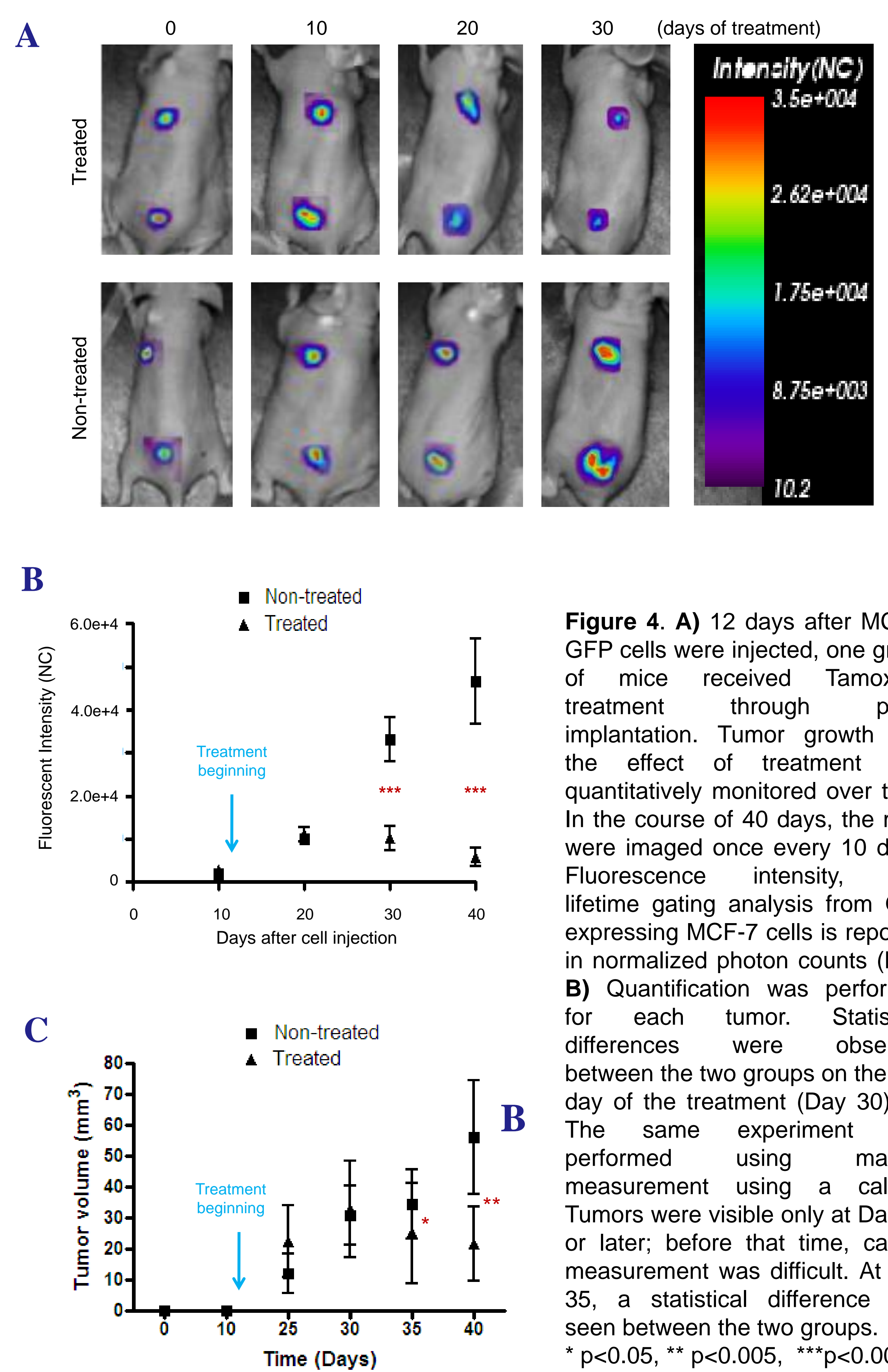
2. Lifetime Gating Analysis Reduces Variability



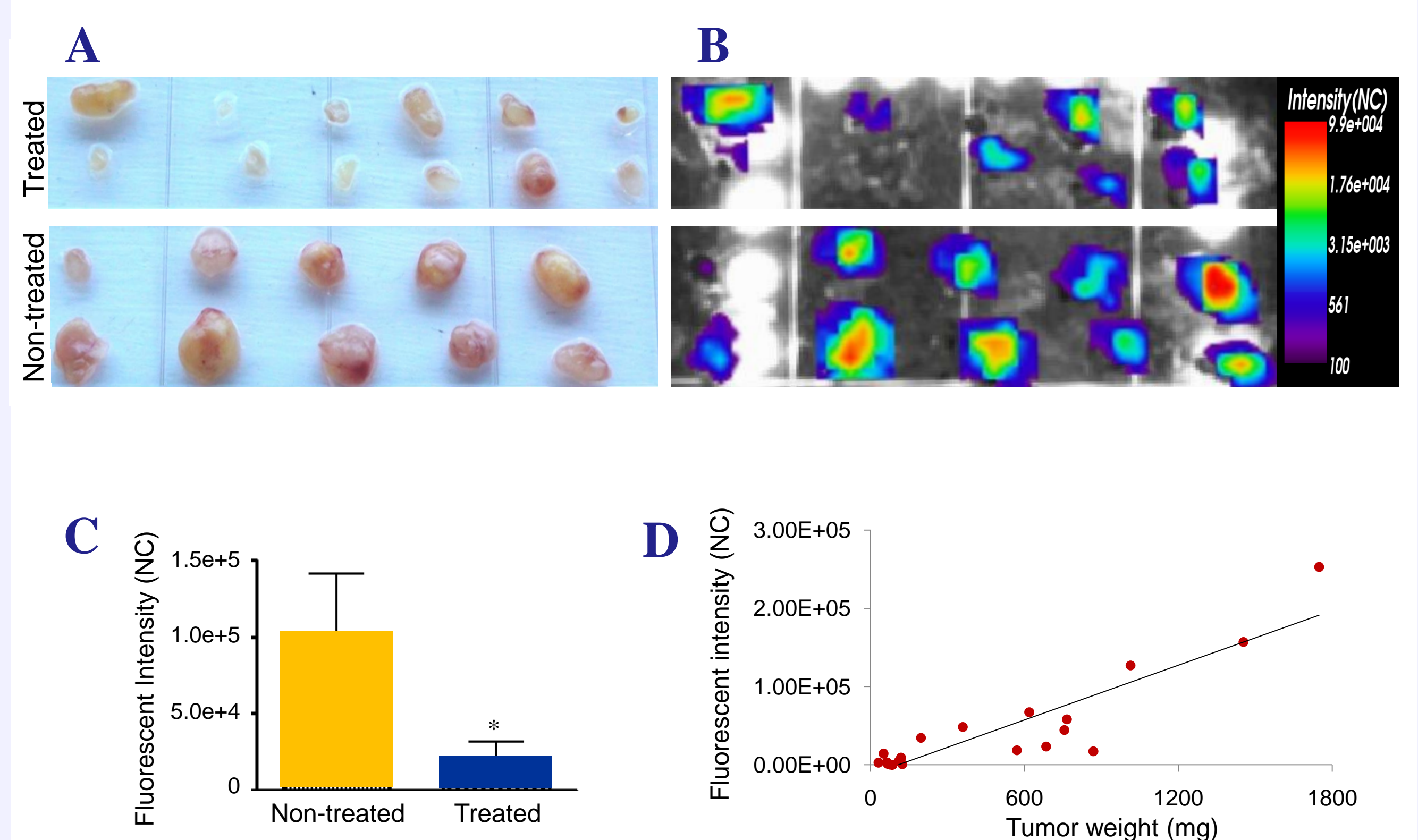
3. Non-Palpable Tumor Detection



4. Monitoring of Tamoxifen Treatment



5. Ex Vivo Imaging



Summary and Conclusions

- We present an advanced method using the Optix MX2 system and fluorescence lifetime imaging to detect, quantify, and assess the effectiveness of treating MCF-7 tumors.
- Fluorescence lifetime gating enables us to eliminate tissue autofluorescence in measured GFP fluorescent signal.
- Elimination of autofluorescence from the measured GFP signal by fluorescence lifetime imaging improves the accuracy of data analysis.
- Using fluorescence imaging, we are able to detect all non-palpable tumors as early as 10 days after implantation of 2 million tumor cells.
- Compared to caliper measurement, GFP fluorescence lifetime imaging is more effective in monitoring treatment, i.e. detecting treatment efficacy earlier.

References

- JR Mansfield et al., *J Biomed. Opt.* 10, 41207 (2005).
- G Ma, et al., *Appl. Opt.* 46, 1650 (2007).