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# Towards Quantitative ICG Angiography: Fluorescence Monte Carlo Multi Cylinder

**Abstract:** Intraoperative blood flow measurement is an effective way to assess the quality of bypass surgery. Flow quantification from indocyanine green (ICG) angiography promises to be an easy, contact-free method. It shows deviations compared to a reference. These are given as factor $k$, which depends on the vessel diameter $d$. The radiation transport within the vessel while recording the ICG passage might cause this. It is analyzed *in silico* to disclose its impact on $k\,(d)$. A Fluorescence Monte Carlo Multi Cylinder (FMCMC) model was developed as a static model, assuming homogeneous concentration of ICG. In contrast to published approaches utilizing a Monte Carlo Multi Layer (MCML) model assuming the deepest penetration location within a photon packet's path to be the fluorescence location, the events are modeled. Fluorescence event modeling, Multi Cylinder geometry and a homogeneous illumination as well as combinations of these were implemented in separate aspect models. Resulting $k\,(d)$ were compared to $k\,(d)$ from MCML. Deviations in $k\,(d)$ derived from FMCMC and MCML in each aspect model were present. The Root Mean Square Error ranges from 6,8% to 36 %, $k\,(d)$ also varied comparing the aspect models to each other. The model geometry, the modeled fluorescence location and illumination mode show a clear impact on simulated $k\,(d)$. Therefore, our study shows that simplifications of previous studies are invalid. The developed FMCMC model considers the named aspects, allowing the analysis of radiation transport in ICG angiography. The FMCMC model assumes a homogeneous concentration of ICG which is not true in clinical cases. Obtaining the heterogeneous distribution of ICG is possible via fluid flow models. Coupling the fluid flow model and the developed radiation transport model as well as including a detailed camera optic is the task for future work.

**Keywords:** Monte Carlo model, ICG angiography, blood flow measurement, intraoperative video processing

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## 1 Introduction

Intraoperative blood flow measurement is performed to evaluate the success of cerebral revascularization surgery. State-of-the-art techniques are based on ultrasonic solutions; their application implicates the risk of tissue damage, infection and interrupts the surgeon's workflow. Alternative methods are taken into consideration. This work focuses on the volume flow quantification from contact free recorded indocyanine green angiography. Assuming the recorded bolus velocity to be equal to the mean blood velocity $\overline{v}$, Weichelt et al. [1] quantified the blood volume flow $\dot{V}_{opt}$ in a single vessel as shown in (1), where $A$ is the vessel's cross-section area, $\overline{v}$ the recorded flow velocity, $d$ the vessel inner diameter and $\Delta t$ the transit time the bolus takes to travel a distance $s$.

$$\dot{V}_{opt} = A \cdot \overline{v} = \pi \cdot \left(\frac{d}{2}\right)^2 \cdot \frac{s}{\Delta t} \tag{1}$$

The optical results were compared to the results of a reference measurement $\dot{V}_{true}$, derived from an ultrasonic flow probe. Deviations are quantified as factor $k$:

$$k = \frac{\dot{V}_{opt}}{\dot{V}_{true}} \tag{2}$$

Using a set of silicone tubes with varying diameters, Weichelt et al. found $k$ is correlated with $d$ [1]. A research project in Karlsruhe systematically analyzes $k\,(d)$. Errors occurring in vessel segmentation and extraction of geodesic length $s$ and diameter $d$ do not cause $k\,(d)$ as shown in [2]. Consequently, the bolus transit time $\Delta t$ is analyzed. In particular, the authors question the assumed equality of the recorded dilution curve velocity and the blood mean velocity. The blood flow within the vessel is assumed to be laminar, a critical discussion can be found in publications like [3]. It is valid for large peripheral arteries. The blood volume flow is calculated, normalizing to mean velocity $\overline{v}$:

$$\dot{V}_{true} = \int_A v(r,\varphi)\ dA = \overline{v} \cdot \int_A v_{rel}(r,\varphi)\ dA \tag{3}$$

Illumination and camera are arranged collinearly. The recorded bolus passage represents a remission measurement. Since vessel wall and blood are highly scattering and turbid media, the illumination intensity over the vessel's cross

section will not be constant. There will be more fluorescence events in brightly illuminated areas. A photon emitted in a fluorescence event far from the camera has a lower probability to be recorded than one emitted in a close event. It can be absorbed within its propagation towards the camera or simply miss it. The contribution to the recorded frame intensities in fluorescence angiography is not expected to be constant over the vessel's cross section. $\omega\,(r,\ \varphi)$, a probability density function, is introduced. It weighs the relative local blood velocity according to its contribution to the total remitted fluorescence intensity. The recorded velocity can be written:

$$\dot{V}_{opt} = \overline{v} \cdot \int_A v_{rel}(r,\varphi) \cdot \omega(r,\varphi)\, dA \tag{4}$$

$$= \underbrace{A \cdot \overline{v}}_{V_{true}} \cdot \underbrace{\int_A \frac{v_{rel}(r,\varphi)\cdot\omega(r,\varphi)}{A}\, dA}_{k} \tag{5}$$

The idea leads to an approximation of $k$ and the underlying statement: The combination of location-dependent blood velocity and weighted intensity lead to an observed velocity differing from the blood mean velocity and therefore cause the deviation $k\,(d)$. Due to its dynamic nature, it is analyzed *in silico*. $\omega\,(r,\ \varphi)$ is obtained from a Monte Carlo model of photon propagation in turbid media. Several models allow the assessment of fluorescence or photon propagation within several geometries, but - to our best knowledge - there is no model assessing fluorescence in a Multi Cylinder geometry. A Fluorescence Monte Carlo Multi Cylinder (FMCMC) model is developed and validated to assess $\omega\,(r,\ \varphi)$ accurately.

# 2 FMCMC Model

The Fluorescence Monte Carlo Multi Cylinder (FMCMC) model is based on the Monte Carlo Multi Layer (MCML) model presented by L. Wang and S. L. Jacques in 1995 [4]. Radiation is represented by numerous photons, the wave character of the light is neglected. The propagation of photons is simulated based on Monte Carlo methods, physical quantities like reflectance are scored. Simulating numerous photons, the scored quantities converge. In FMCMC model, the model geometry was adapted to reflect radiation transport within a vessel and fluorescence events were modeled.

Some central assumptions were made: Absorption coefficients and scattering coefficients are assumed to be constant for blood and vessel wall. Fluorescence events induced by photons emitted in a prior fluorescence event are neglected. Absorption and emission in a fluorescence event occur without time delay. The vessel's geometry is approximated to be a cylinder (blood), surrounded by a hollow cylinder (vessel wall).

## 2.1 Model Geometry and Illumination

The photon location and direction in FMCMC was modeled in cartesian coordinates $x, y, z$. The scoring of fluorescence events was done in a polar grid system $(r, \varphi, y)$ to avoid overlapping bins at the boundaries. The coordinate system applied is visualized in Figure 1. Note, the origin's location is at the $y$-axis, which is the axis of symmetry.

Launching every photon packet at $(x = 0, y = 0, z = 1)$ in negative z-direction models a single point illumination. Launching the photons at $(x = a, y = 0, z = \sqrt{1 - a^2})$, choosing a random $a$ in the range of the cylinder radius $r$, $-r < a < r$ models a homogeneous illumination.

Checking for boundary hits within propagation steps was simplified by orthogonal projection to the x-z-plane. Considering the propagation step as part of a straight line and the boundaries as circles, their intersection can be easily found. If a boundary hit occurs, reflection and refraction are modeled applying a random number, comparing it to the reflected portion calculated using Fresnel equation as in [4] and applying ray tracing algorithms from [5]. The photon packets are reflected or refracted, but not split.

## 2.2 Fluorescence Model

Fluorescence events are modeled as it was described by Welch et al. [6]. This approach was chosen since its implementation is convenient and the model is independent from symmetries, exact camera models and shape of single bins.

A fixed weight Monte Carlo photon propagation model simulates the excitation photon's path. When absorption occurs, a photon packet is started from this exact point of absorption in a random direction. The initial weight equals the product of the absorption coefficient of the fluorophore normed to the total absorption coefficient and the fluorophore's quantum yield. This simulates the number of photons remitted in a fluorescence event absorbing the excitation weight of 1.

The concentration of the fluorophore is assumed to be constant over the vessel cross section, so are the optical parameters. The fluorescent intensity coming from one bin, normalized to the total remitted intensity is of interest regarding $k\,(d)$. The fluorophore's quantum yield and absorption coefficient do not influence k, the scaling of the intensity from each bin and the total remitted intensity cancel each other out. So, the parameters are randomly chosen but constant. This is done in agreement with Welch et al. [6]

Note: The choice of random, constant parameters models a homogeneous fluorophore concentration!

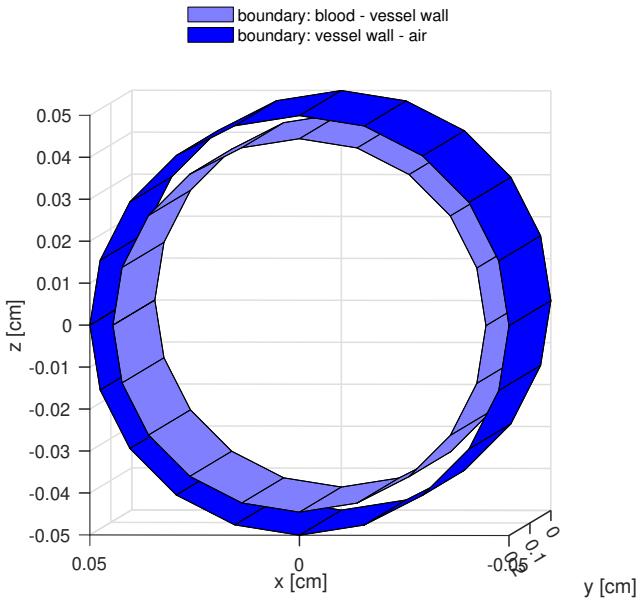


**Figure 1:** Geometry and cartesian coordinate system in Multi Cylinder geometry. A polar grid ($r$, $\varphi$, y) in the evaluation of fluorescence events avoids overlap of bins at the boundaries.

# 3 Verification – Model Geometry

The model geometry is correctly modelled if boundary hits in the photon propagation path are processed correctly. The detection of boundary hits, the reflection, transmission, illumination and grid registration functions were verified separately. The verification of boundary hit detection is presented exemplarily:

One million valid scenarios were analyzed. Random start- and endpoints of one single photon step were chosen as well as a random set of cylinder radii. The scenario was only considered valid if a boundary hit occurred. Its position was examined applying the presented projection approach and an iterative approach, depicting the photon step as a number of single points in a straight line. The distance of each point to each boundary was calculated. Distances under a threshold were analysed, the smallest distance was considered to be the boundary hit location. Each of the one million scenarios showed close hit locations, negligible deviations are expected due to the iterative approach. Reflection, refraction, grid registration and illumination were verified analogously.

# 4 Validation – Fluorescence

The fluorescence model was validated based on data reported by Liu et al. [7]. Their publication reports findings in two phantom sets made of water, ink, small polystyrene spheres and fluorescent dye. One set had a fixed scattering and a variable absorption coefficient, the other set the other way round. They used multiple fiber optic geometries to measure the remitted fluorescence intensity in all phantoms.

The validation experiments were modeled applying a single layer Monte Carlo model. One fiber optic setup was modeled. The fluorescence intensities are presented in Figure 2. Deviations of up to 25% comparing the experimental data and the fluorescence model based on Welch's algorithm were found. This accuracy is acceptable; the comparison of several fluorescence models will be a task for future work.

Note: It is assumed that fluorescence locations are modeled accurately if the total remitted fluorescence in experiments and model matches.

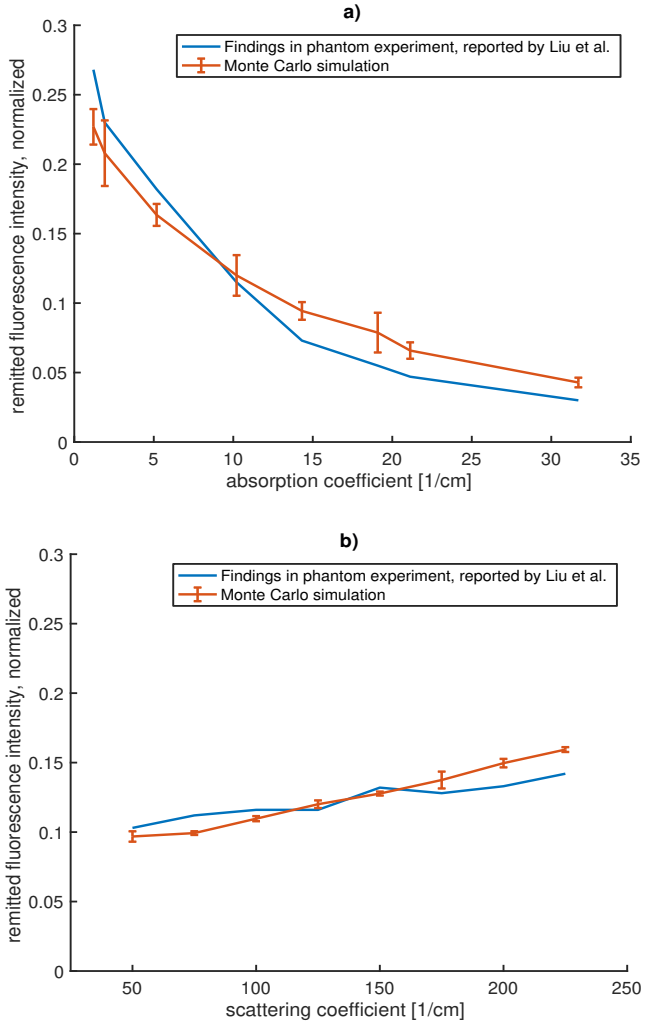


**Figure 2:** Fluorescence intensities from Monte Carlo models are similar to the findings reported by Liu et al. [7]. The range of 5 simulations is shown, 1.000.000 photons/datapoint were analyzed. In a), the absorption coefficient and in b), the scattering coefficient was varied.

# 5 Comparison to MCML

In previous works, the deepest penetration location within a photon packet's path was assumed to be the location of fluorescence and therefore the origin of recorded intensity. A MCML model tracking these deepest locations of every simulated photon packet was applied to evaluate $k\,(d)$. Several aspects differentiate FMCMC and the previously applied MCML: The model geometry, the assumed origin of recorded intensity and the modeled illumination.

The application of the MCML model neglects noteworthy impact of the differentiating aspects on $k\,(d)$. It implies that MCML geometry, the assumed origin of recorded intensity and illumination mode reflect the radiation transfer in a fluorescence angiography scenery appropriately. The authors question this. $k\,(d)$ obtained from MCML and FMCMC are compared. Clear differences in $k\,(d)$ depict the proof that assumptions made in previous works are not valid.

The differentiating aspects are implemented in separate aspect models to allow the assessment of their impact on $k\,(d)$ in comparison to the previously applied MCML model. Absorption and scattering coefficients as well as the fluorophore's parameters are kept constant. Since bin shapes and sizes differ, the resulting $k\,(d)$ is comparable, but not the spatial distribution itself. The normalized velocity profile does not change, so variance in $k\,(d)$ shows variance in $\omega\,(r,\ \varphi)$ in the various aspect models.

Significant de$k\,(d)$viations in approximated based on $\omega\,(r,\ \varphi)$ from the aspect models were found. Since $k$ varies with the choice of $d$, the Root Mean Square Error (RMSE) is calculated to quantify the deviations. The given percentage is calculated dividing RMSE by mean MCML results:
Multi Layer vs. Multi Cylinder: RMSE = 0.403 (38,63%)
Deepest vs. fluorescence location: RMSE = 0,071 (6,84%)
Homogeneous vs. point illumination: RMSE = 0,375 (36,00%)

# 6 Conclusion

The Fluorescence Monte Carlo Multi Cylinder model overcomes the neglection of impacts from model geometry, assumed fluorescence location and illumination stated in previous work. The presented model is a step towards the accurate simulation of transit time deviations in fluorescence angiography. Understanding these deviations will allow the optical measurement of volume flow based on fluorescent dyes like ICG. Its advantages in the intraoperative setting are obvious, it might be beneficial in hazardous environments like the chemical industry as well.

# 7 Outlook

The FMCMC model reflects the impact of radiative transfer in ICG angiography *in silico*. However, a constant fluorophore concentration was assumed, which is not true in clinical cases. In addition, it is inconsistent with the assumed laminar flow profile. Obtaining the spatially heterogeneous concentration profile of ICG is possible via fluid flow models. Coupling of the fluid flow model and the developed FMCMC model will be a task for future work. This allows the assessment of the bolus transit time in an appropriate spatial and temporal resolution *in silico*.

A detailed camera model should be implemented in future works. Investigating the impact of its details, size and distance to the model on $k\,(d)$ promises additional insight. The comparison of the performance of multiple fluorescence models is a task for further studies.

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