

# Estimation of breast tumour tissue diffusion parameters from histological images and Monte-Carlo simulations

David Naves Sousa<sup>1</sup>, Filipa Borlinhas<sup>1</sup>, and Hugo Alexandre Ferreira<sup>1</sup>  
Institute of Biophysics and Biomedical Engineering, Faculdade de Ciências da Universidade de Lisboa, Portugal

## Introduction

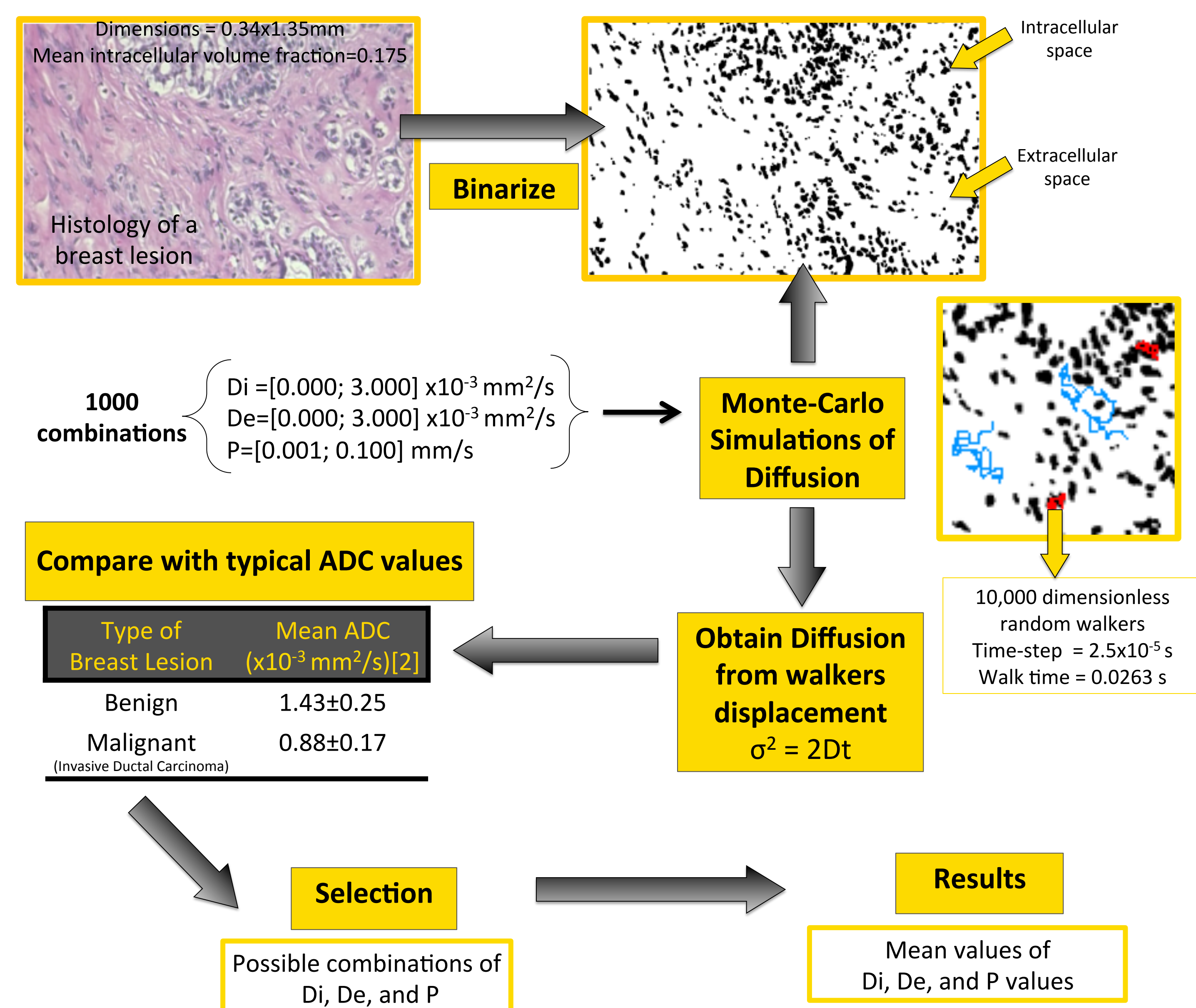
- Diffusion Weighted Magnetic Resonance Imaging (DW-MRI) can differentiate between benign and malignant breast tumours using Apparent Diffusion Coefficient (ADC) [1,2].
- ADC is not able to estimate the intracellular diffusion ( $D_i$ ), extracellular diffusion ( $D_e$ ) and Permeability ( $P$ ) values of the lesions.
- Monte-Carlo Simulations (MCS) of diffusion processes have shown to be useful in characterizing simulated histological environments at the microstructural level [3].

## Purpose

Estimate combinations of  $D_i$ ,  $D_e$  and  $P$  values that could explain the observed ADC values using MCS on real histological images of benign and malignant breast tumors and thus further characterise tumour tissues.

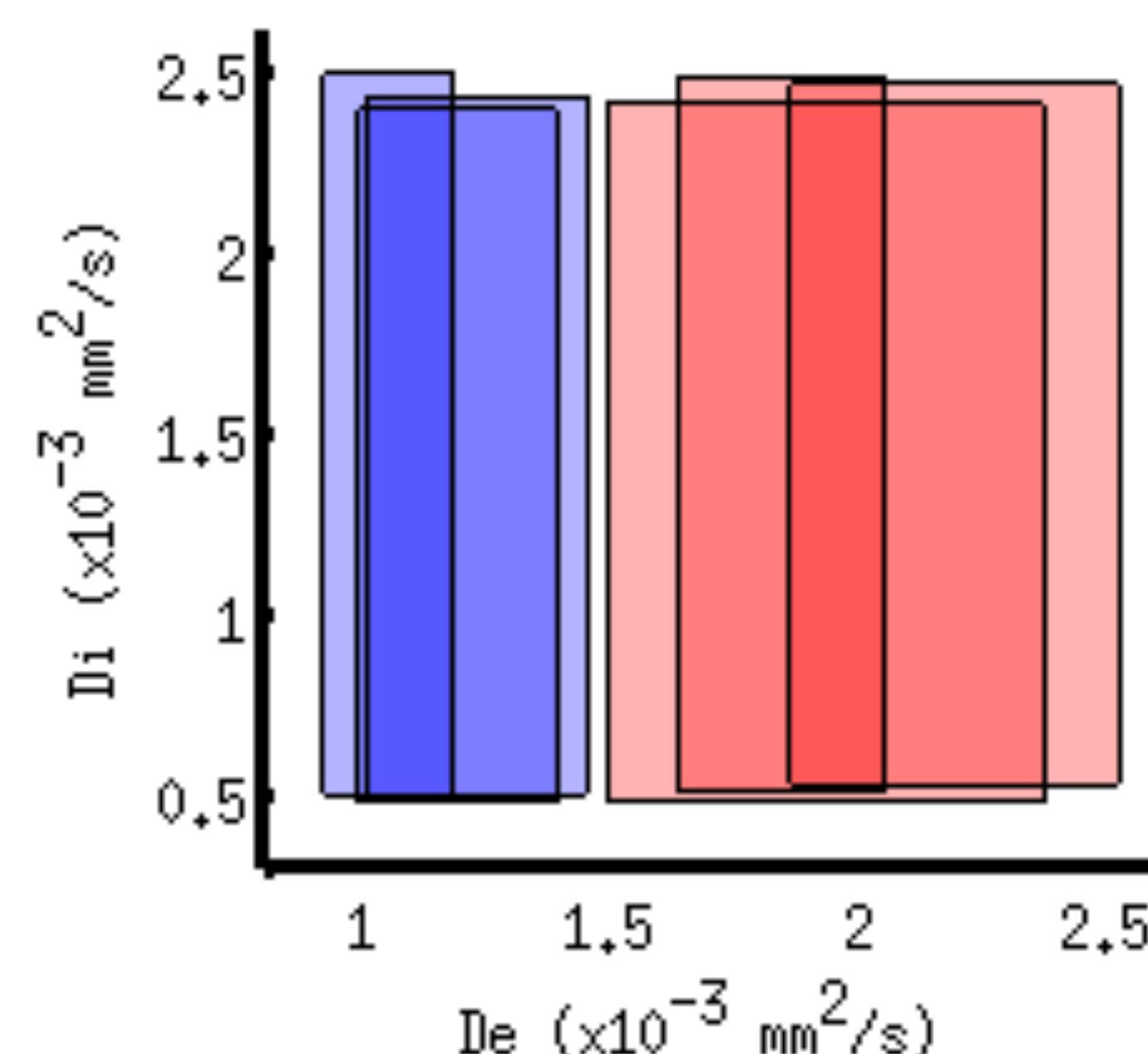
## Methods

Histological images of benign ( $n=3$ ) and malignant ( $n=3$ ) breast tumours were analysed [4]. The applied methodology is shown in the fluxogram:



## Results and Discussion

- Figure 1 shows the ranges of possible combinations obtained for  $D_i$  and  $D_e$ .
- Distinct values of  $D_e$  correlate with the breast tumor type (Table 1 and 2).
- The presented approach is able to translate changes in the extracellular medium but is not sufficiently sensitive to depict significant changes in  $D_i$  and  $P$  (Table 1), which could be expected. This may be the result of the low number of images studied and, especially, of the oversimplified processing of the histological images (binarisation only) prior to MCS.



	$D_i$ ( $\times 10^{-3} \text{mm}^2/\text{s}$ )	$D_e$ ( $\times 10^{-3} \text{mm}^2/\text{s}$ )	$P$ (mm/s)
B1	1.48±0.96	2.19±0.33	0.050±0.031
B2	1.44±0.96	1.93±0.44	0.050±0.031
B3	1.49±0.98	1.84±0.21	0.050±0.031
M1	1.43±0.95	1.19±0.20	0.048±0.030
M2	1.39±0.99	1.05±0.13	0.047±0.033
M3	1.46±0.96	1.23±0.22	0.054±0.029

**Figure 1.** Representation of the ranges of possible ( $D_i, D_e$ ) combinations for each histological image. Benign tumours in red, malignant tumours in blue.  $D_i$  – Intracellular Diffusion;  $D_e$  – Extracellular Diffusion.

**Table 1.** Average±standard deviation values obtained for  $D_i$ ,  $D_e$  and  $P$  from the tested combinations of these parameters in the MCS for each histological image. B1 to B3 – Benign breast lesions considered. M1 to M3 – Malignant breast considered.  $D_i$  – Intracellular Diffusion component.  $D_e$  – Extracellular Diffusion component.

Diffusion component	Type of breast lesions		Biological Correspondence
	Benign	Malignant	
$D_e$	Higher	Lower	Higher cellularity [5] of malignant lesions increases the number of barriers for water diffusion in the extracellular medium, consequently reducing the diffusion coefficient of this compartment

**Table 2.** Differences obtained for extracellular diffusion component for benign and malignant breast lesions, and the respective biological correspondence.  $D_e$  – Extracellular Diffusion.

## Conclusion

Distinct combinations of ( $D_i$ ,  $D_e$ ,  $P$ ) are associated with each tumour type.  $D_e$  revealed to be very distinct for benign and malignant tumors in agreement with known extracellular matrix differences.

## References

- [1] Guo Y, Cai Y-Q, Cai Z-L, et al. Differentiation of Clinically Benign and Malignant Breast Lesions Using Diffusion-Weighted Imaging. *J Magn Reson Imaging*. 2002;16:172–8.
- [2] Borlinhas F, Ferreira HA. Quantificação por imagem ponderada em difusão (DWI) das lesões tumorais da mama - Quantitative diffusion-weighted imaging (DWI) in breast cancer. *Saúde Tecnol*. 2012;(October):24–30.
- [3] Lee C-Y, Bennet KM, Debbs JP. Sensitivities of statistical distribution model and diffusion kurtosis model in varying microstructural environments: a Monte Carlo study. *J Magn Reson*. 2013; 230:19–26.
- [4] Spanhol F, Oliveira LS, Petitjean C, et al. A Dataset for Breast Cancer Histopathological Image Classification. *IEEE Transactions on Biomedical Engineering (TBME)*, accepted for publication.
- [5] Hanahan D, Weinberg RA. Hallmarks of cancer: The next generation. *Cell*. 2011;144(5):646–74.
- [6] Conklin MW, Keely PJ. Why the stroma matters in breast cancer: insights into breast cancer patient outcomes through the examination of stromal biomarkers. *Cell Adhesion & Migration*. 2012; 6(3):249–260.