Developing virtual tumors using spherical harmonics and quantitative MRI data

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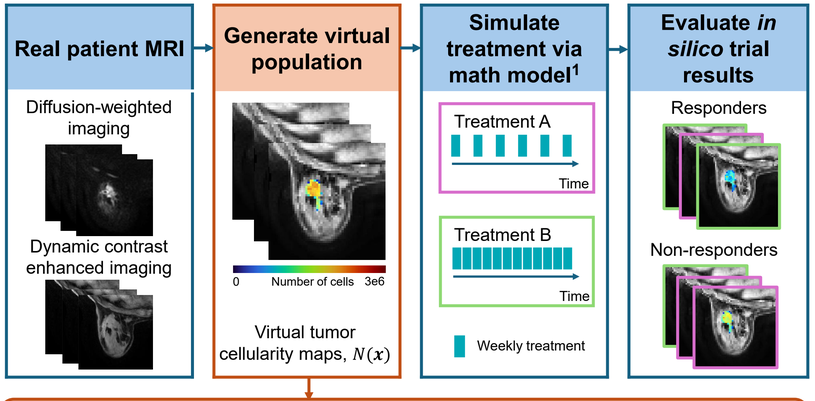
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Abstract: 989
Dec 9-12, 2025

Accelerating clinical trials

In silico clinical trials are a method for accelerating and derisking traditional clinical trials by enabling:

- Evaluation of treatments in large, heterogeneous populations
- Parallel evaluation of multiple treatments in the same patient



To enable *in silico* trials, we present a framework for generating realistic and heterogeneous virtual tumors.

Image processing

Dataset: 27 triple negative breast cancer patients from I-SPY2[2]

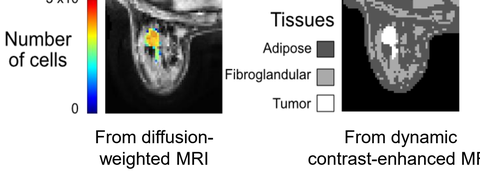


Fig 1. Tumor regions were identified using dynamic contrast-enhanced MR scans[3]. Tumor cellularity maps, $N(x)$, were derived from diffusion-weighted MR scans.[3]

Generating virtual tumors

Virtual tumors were generated using the spherical harmonics (SH) expansion[4] coefficients of pretreatment $N(x)$ maps ("real tumors"). SH expansion describes each $N(x)$ as a set of coefficients; distributions of these coefficients were sampled to generate virtual tumors.

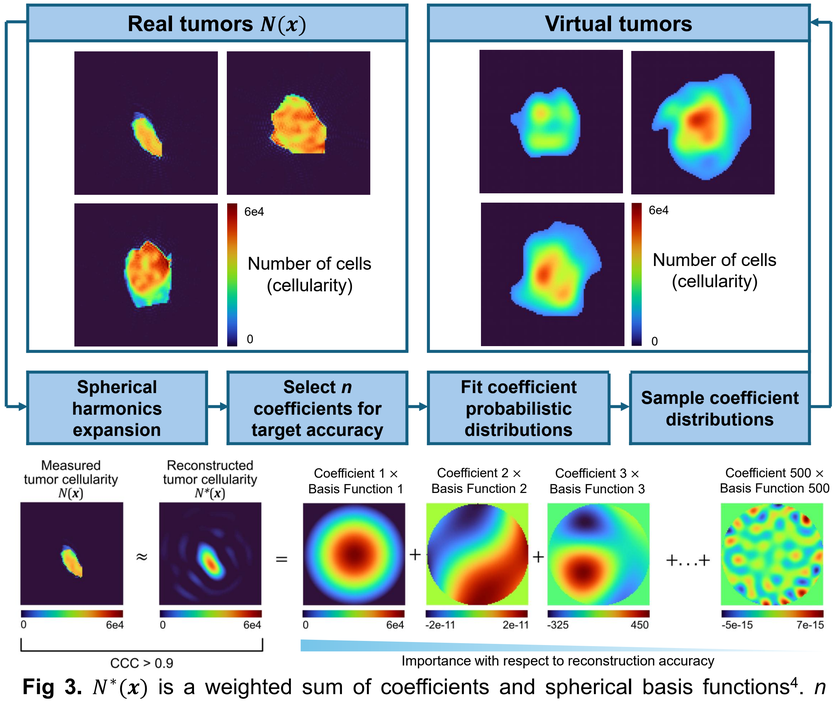


Fig 3. $N^*(x)$ is a weighted sum of coefficients and spherical basis functions[4]. *n* basis functions were used to achieve CCC > 0.9 between $N(x)$ and $N^*(x)$.

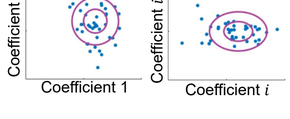
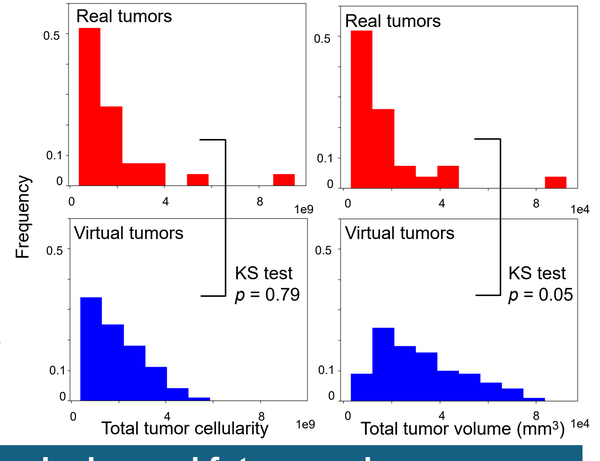


Fig 4. 2D normal distributions were fit to coefficients corresponding to pairs of consecutive basis functions. Sampling the *n*/2 distributions generates *n* coefficients which parameterize a virtual tumor.

Results

We generated virtual tumors similar in total tumor cell number as real tumors.

- 252,279 basis functions (CCC=0.99)
- 500 basis functions sufficient (CCC=0.92)
- 100 virtual tumors generated by sampling 250 distributions times
- Kolmogorov-Smirnov test indicates cellularity distributions are statistically similar.



Conclusion and future work

Using our spherical harmonics-based framework, we generated virtual tumors that preserved the tumor cellularity of the historical population but allowed for variation in tumor volume.

In the future we will:

- Improve distribution fitting to accurately capture tumor volume distribution of historical population
- Conduct *in silico* trials to recreate historical trial results

References

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Acknowledgements

NSF DMS 2436499, NSF DMS 2309782, NSF CISE-IIS 2312746, CPRIT RP220225
This material is based upon work supported by the National Science Foundation Graduate Research Fellowship under Grant No. DE2137420