APPENDIX

A. Implementation details

The algorithm follows a coarse-to-fine process that first estimates parameters at a coarse spatial image resolution level and then updates the solution to a finer resolution level. We applied a multi-resolution scheme with 3 resolutions levels; two levels in which the joint problem is solved and one at full image resolution in which only the appearance model is optimized, keeping the previously obtained deformation fields fixed. A fast optimization scheme relying on linear programming and duality [1] is used at each step. Finally, regarding the run-time performance of the method, all the experiments were computed on a 8-cores machine (3.6 GHz processing power) with a memory requirement of 4 GB. It took approximately 26 minutes to co-register the images of a sequence of size of five (five DW images), using five sub-iterations in each pyramidal level for refining the label space. The number of sub-iterations to be used is a factor that heavily affects the computational time of our method.

B. Calculation of Optimal Weights of Potentials

The optimal values for the weights (λ) on the potentials of the energy function were computed using simulated data and simulated deformation fields. Details on the simulation process are provided later in subsection E of the *Methods* section in the main manuscript. Let's denote the matrix of the potentials by V. We found the optimal weights on these potentials for each registration method by solving the following linear least-squares problem:

$$c_{opt} = \min_{c} \frac{1}{2} \|V \cdot c\|^2, \tag{B.1}$$

subject to $\sum_{n=1}^{N} \lambda_n = 1$, $\lambda_n > 0$, where $c = [\lambda_1 \ldots \lambda_N]$ the vector of the weights. In that way, we avoid learning the weights through brute force by running the same experiment many times, which would be a computationally costly approach.

C. Euclidean Distance Metric

The Euclidean distance (ED) was used as a distance criterion for evaluating how close to the simulated deformation fields were the ones derived by each method, with the mean distance over the entire image region Ω being $ED_t = \frac{1}{|\Omega|} \sum_{x \in |\Omega|} \|D_t(x) - \mathbf{D_t}(\mathbf{x})\|_2$, with $\mathbf{D}(\cdot)$ being the simulated deformation field. Then the averaged over the deformation fields error is $\bar{ED} = \frac{1}{m-1} \sum_{t=2}^{m} ED_t$.

D. Measure of Sum Squared Error

The sum of squared errors of prediction (SSE) was used as a measure to define the discrepancy between two images. In case of comparing the simulated ADC image and the one computed or derived through each of the examined registration methods, the formula for the mean SSE over the entire image region Ω is: $SSE = \frac{1}{|\Omega|} \sum_{x \in |\Omega|} (z(x) - \mathbf{z}(\mathbf{x}))^{\mathbf{2}}$, where z and $\mathbf{z}$ are the estimated by each method ADC map and the simulated ADC map respectively (for example z is derived in case of $JointRef1$ by Eq.(5) in the main manuscript and by Eq.(6) in the main manuscript in case of $MIGroup$). In case of comparing the data fitted by the diffusion model (Eq.1 in the main manuscript), forming image $\mathbf{s_t}(\cdot)$ and the real data (image $s_t(\cdot)$), the mean SSE over the tumor area Ω_t is computed as: $SSE_{mean} = \frac{1}{|\Omega_t|} \sum_{x \in |\Omega_t|} (s_t(x) - \mathbf{s_t}(\mathbf{x}))^{\mathbf{2}}$. The standard deviation of SSE is computed as: $SSE_{std} = \frac{1}{|\Omega_t|} \sum_{x \in |\Omega_t|} ((s_t(x) - \mathbf{s_t}(\mathbf{x})) - \mathbf{SSE_{mean}})^{\mathbf{2}}$ and $SSE_{std} = \frac{1}{|\Omega|} \sum_{x \in |\Omega|} ((z(x) - \mathbf{z}(\mathbf{x})) - \mathbf{SSE_{mean}})^{\mathbf{2}}$ for the two cases respectively.

REFERENCES

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[1] N. Komodakis, G. Tziritas, N. Paragios, Performance vs computational efficiency for optimizing single and dynamic mrfs: Setting the state of the art with primal-dual strategies, Computer Vision and Image Understanding 112 (1) (2008) 14–29.

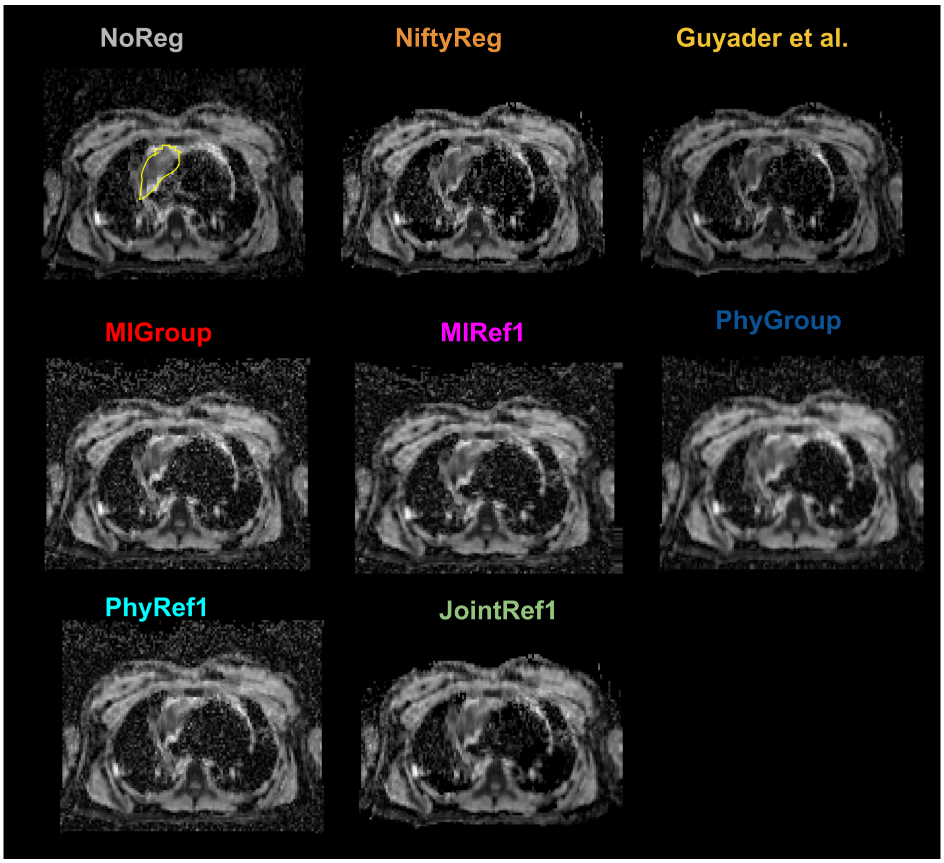

Fig. .1: Same axial slice of the ADC map derived by all examined registration methods. The yellow contour on the first image (up-left) denotes the tumor of the patient, delineated by an expert radiologist.