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TU/e Technische Universiteit Eindhoven University of Technology

Deep learning for medical image registration

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Outline for today:

- First hour:
  - Quick recap of medical image registration
  - Introduction non-parametric / deformable image registration
  - Deep learning for medical image registration:
    - Deep iterative registration
    - Supervised methods
    - Unsupervised (optimization-based) methods

- Second hour:
  - “Guest lecture”
    - Image registration for adaptive radiotherapy
    - Challenges in image registration, e.g., small open-source datasets

Learning outcomes

The student can:

- differentiate between parametric and non-parametric/deformable transformation models.
- explain what a displacement (vector) field is and calculate the corresponding number of free parameters, given a medical image pair to be registered.
- name the main advantages and disadvantages of using deep learning for medical image registration.
- categorize deep learning-based medical image registration methods into one of the three groups of methods based on how they deal with the ground truth displacement.
- For each category, give an example of a method that was proposed in recent literature.

Recap: medical image registration

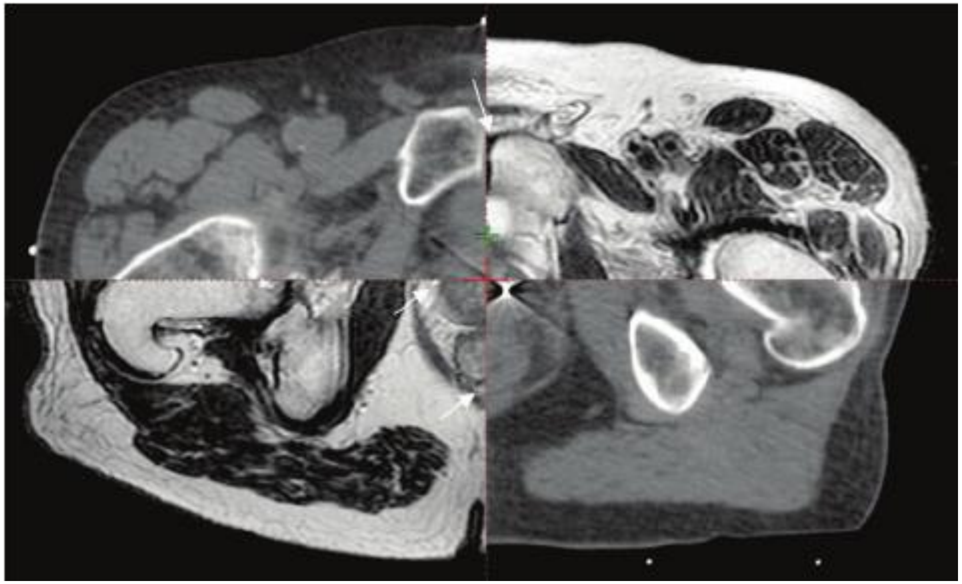
Why important?

- Multi-modal registration (e.g. CT on MRI)
- Inter-subject (e.g. atlas registration)
- Longitudinal (e.g. treatment evaluation)

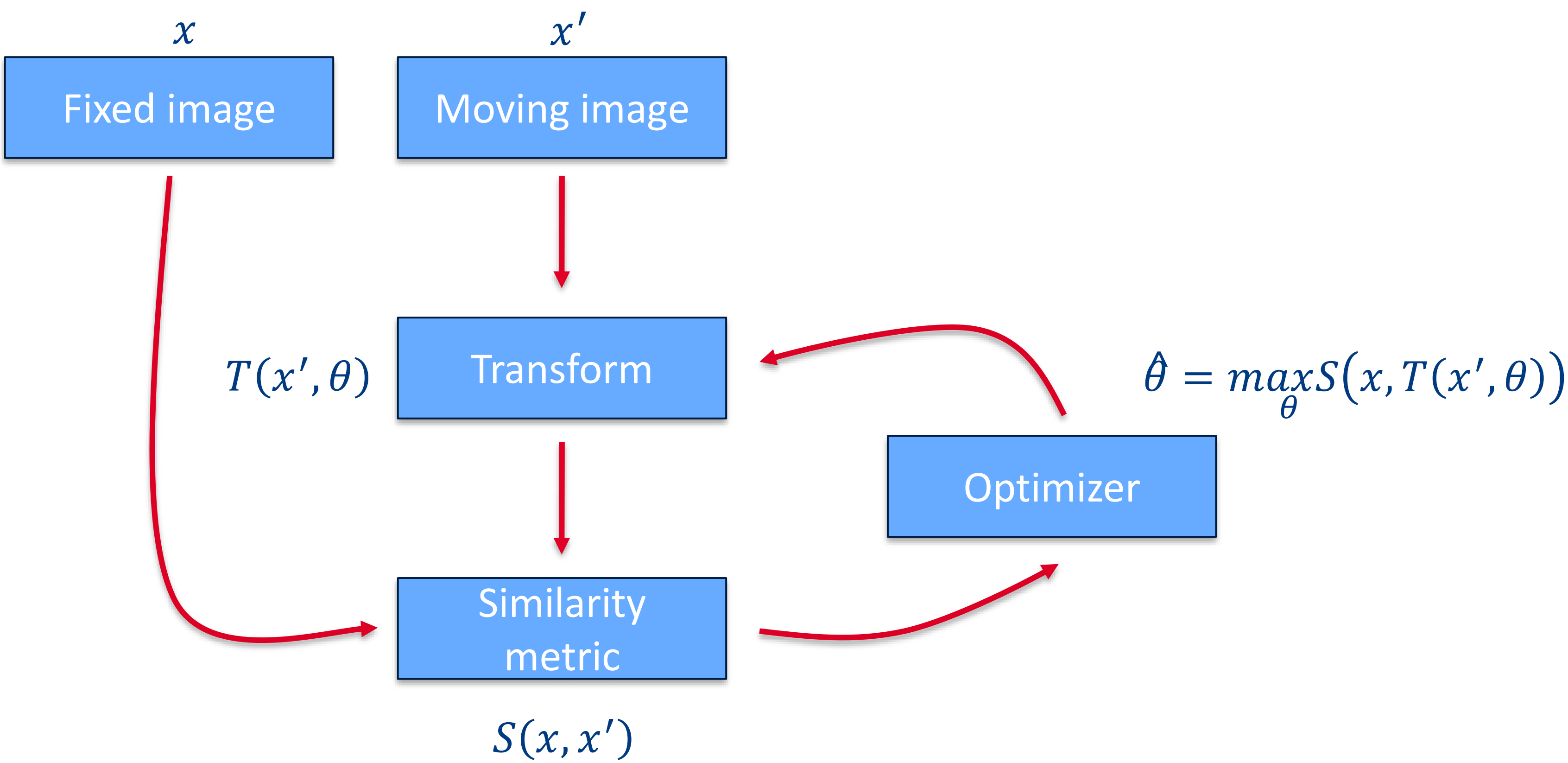
Remaining challenges:

- Large 3D volumes
- Accuracy vs. efficiency

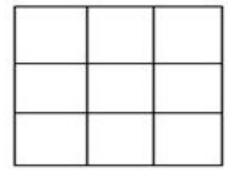
- Intensity inhomogeneities and discontinuities
- Outlier rejection

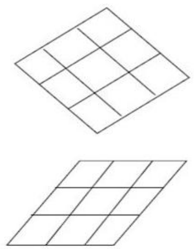


Finding the optimal transformation

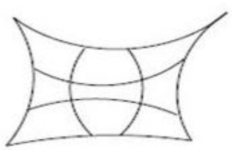


Transformation models

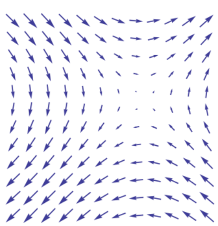




Rigid & Affine
- Point or feature-based (e.g. landmarks, fiducials)
- Intensity-based
- Gradient/edge-based

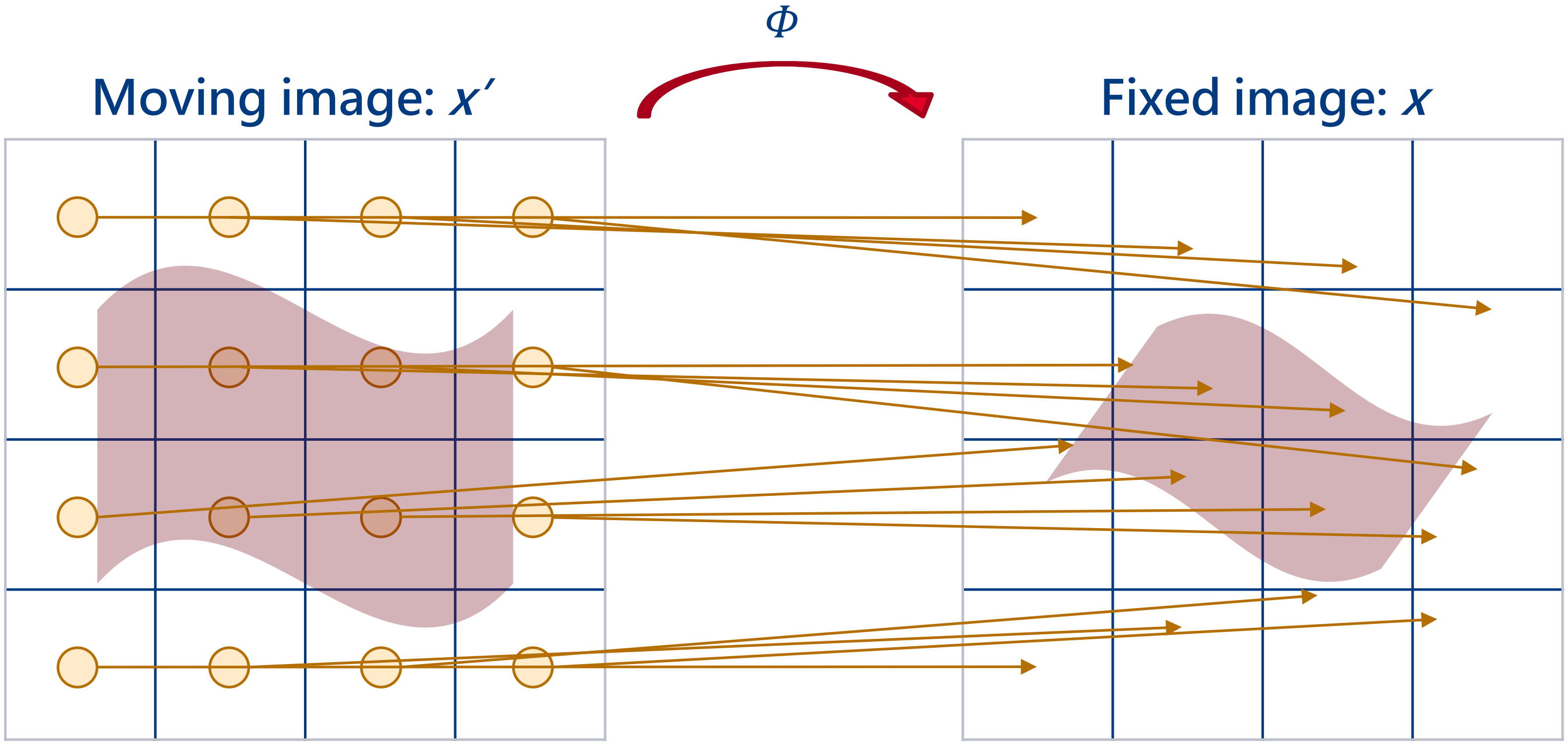


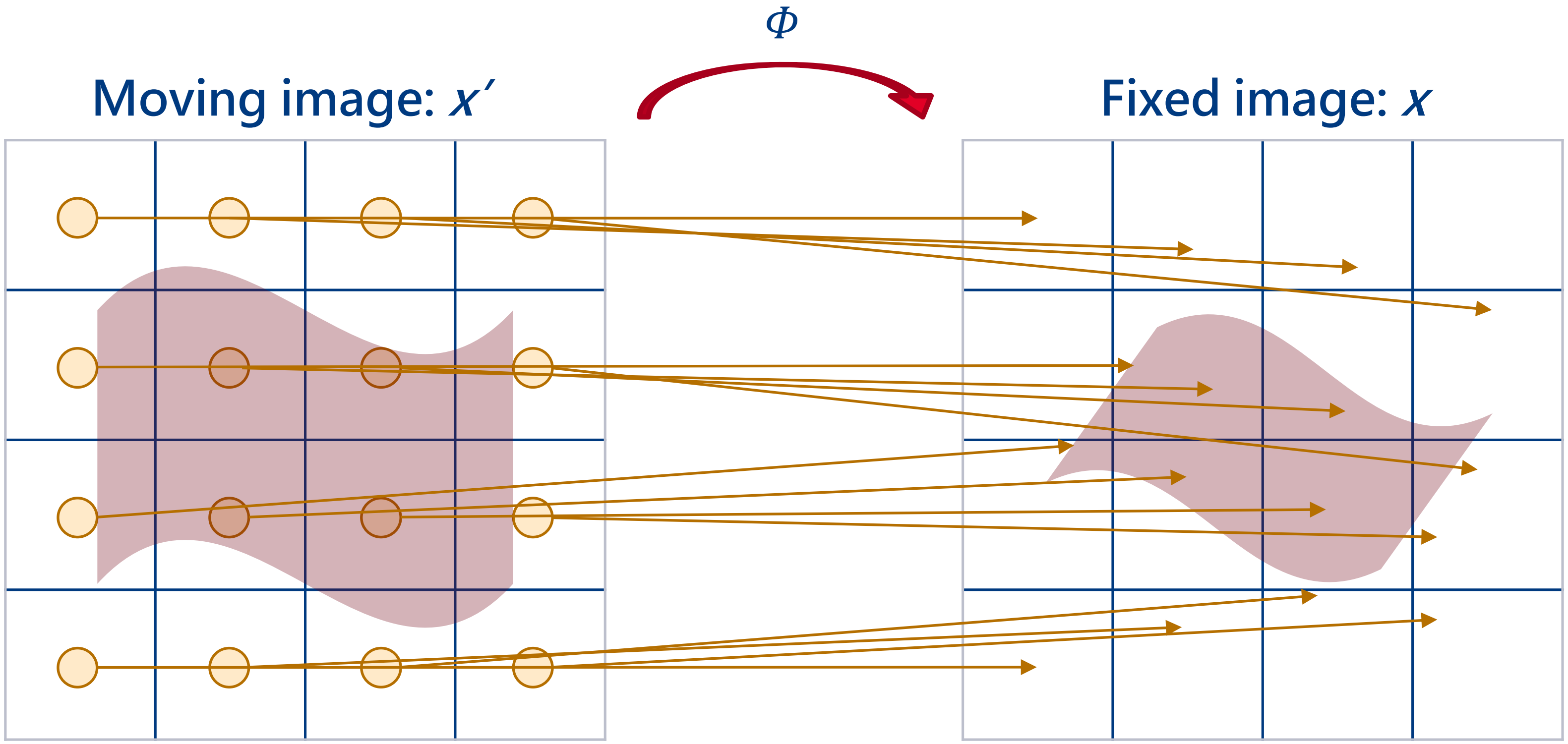
Non-linear
- Linear or higher order polynomials
- Spline-based



Non-parametric / deformable
- Allowing each image element to be displaced arbitrarily

Displacement (vector) field (DVF) = Dense set of vectors representing the displacement in a given spatial domain





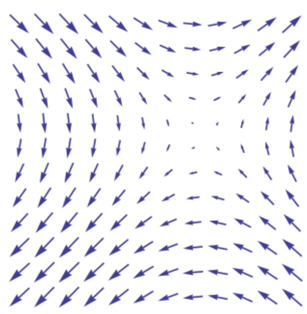
Deformation: $\varphi = Id + u, \varphi: \Omega \to \mathbb{R}^d$

or point-wise: $\varphi(x) = x + u(x)$

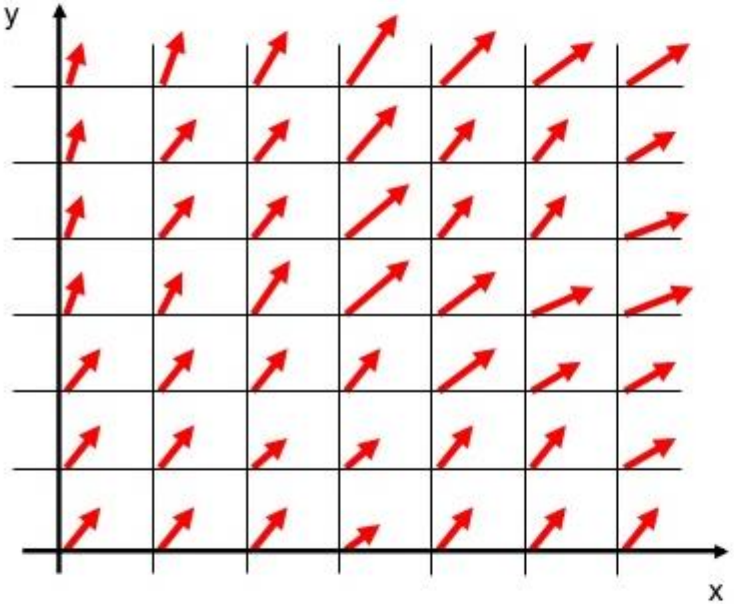
Displacement:

$u: \Omega \to \mathbb{R}^d$

e.g. $u = [u_x, u_y, u_z]$



Deformable image registration: how many free parameters (DOF) in 3D?



Typical spatial resolution of a 3D medical image (MRI: e.g. 1.5×1.5×4 mm^3 voxels)

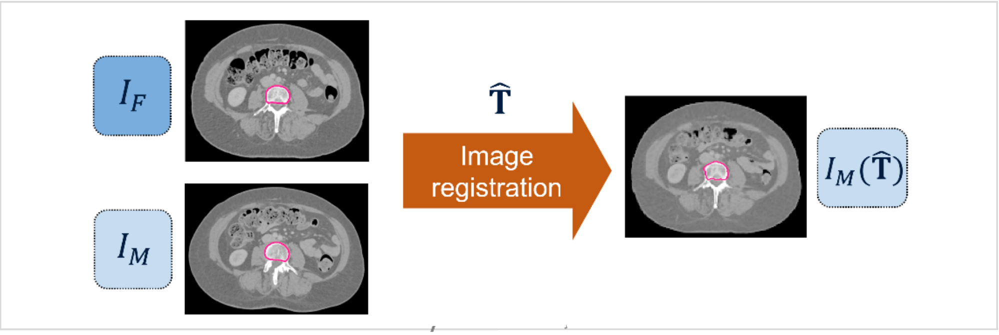
DOF = 3*Nx*Ny*Nz (!)

Deformable image registration is still a very active area of research, and many different deformable registration models exist:

- Free-form deformation model
- Optical flow
- Demons
- Fluid flow
- Diffeomorphisms
- …

Note that the details of these models and their implementations are beyond the scope of this course.

Why focus on deep learning for medical image registration?



Real time applications!

Learning image registration: how does it work?

Problem: how can we obtain the ground truth displacement ?

A. Deep iterative registration

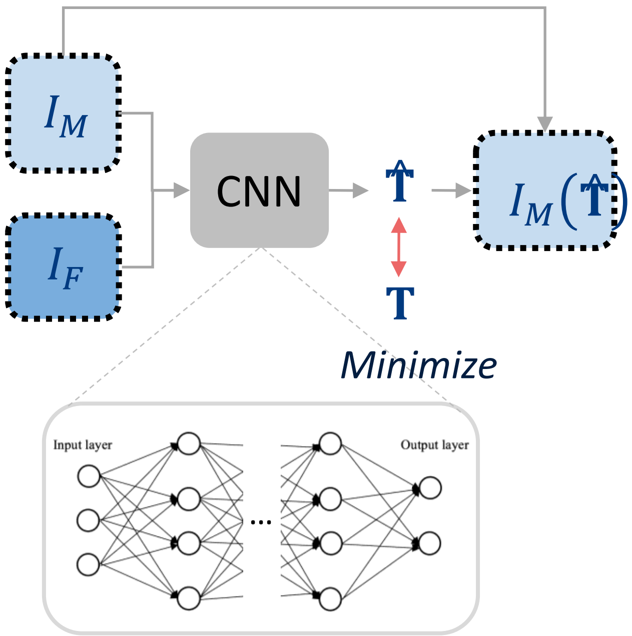
- Learn a component of a classical registration method

B. Supervised transformation estimation

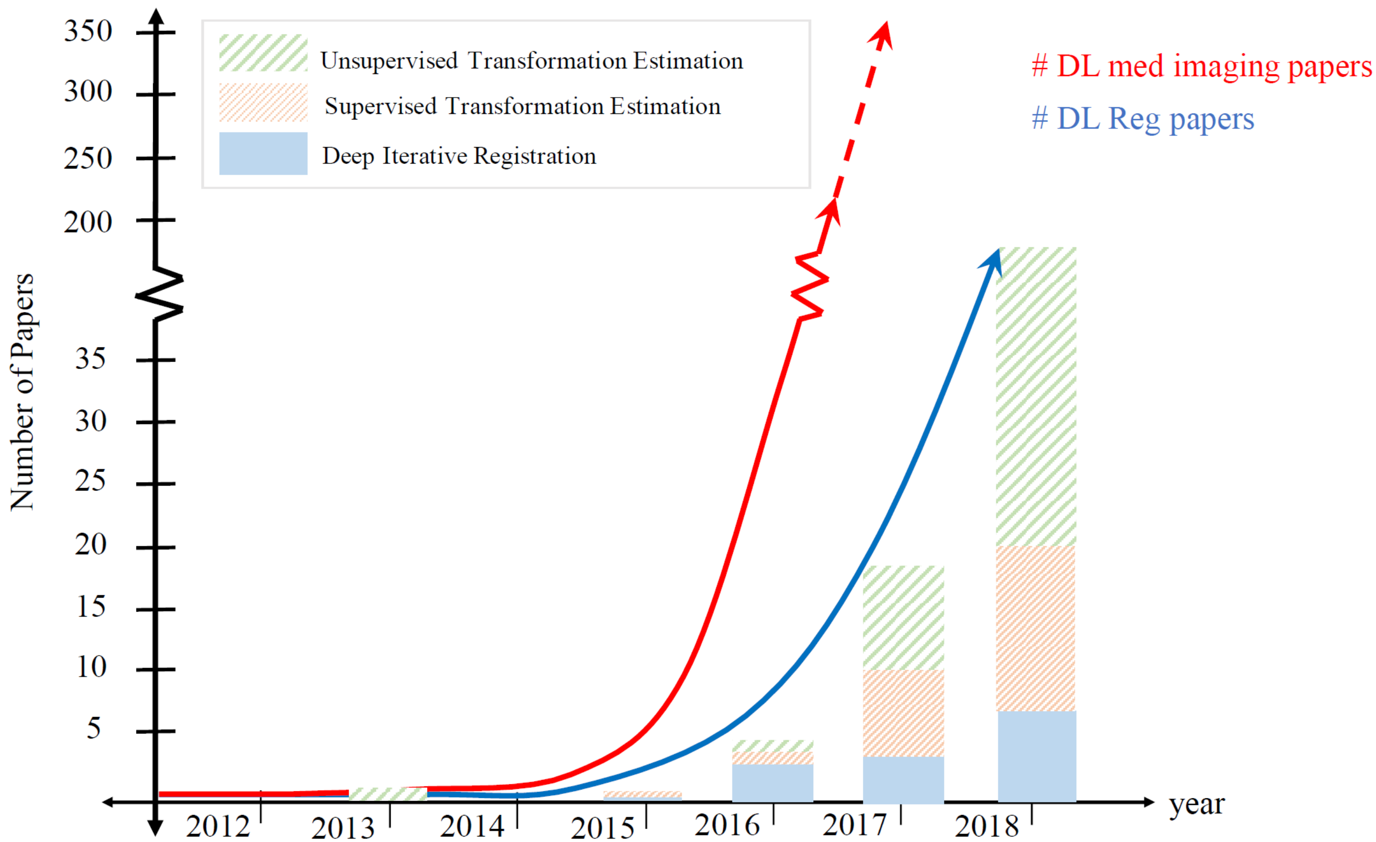
- Obtain using classical registration method
- or make synthetic ground truth

C. Unsupervised transformation estimation

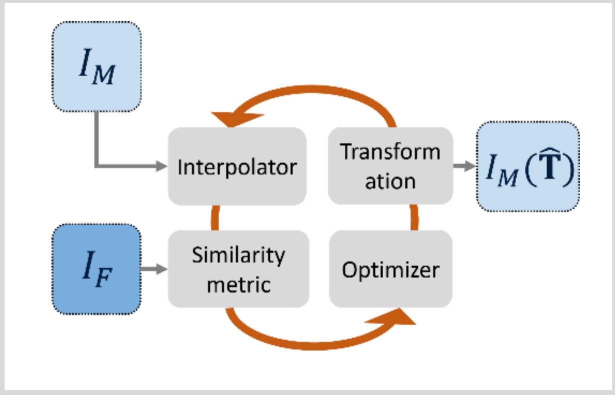
- Use similarity metric to judge



Publications on deep learning for medical image registration



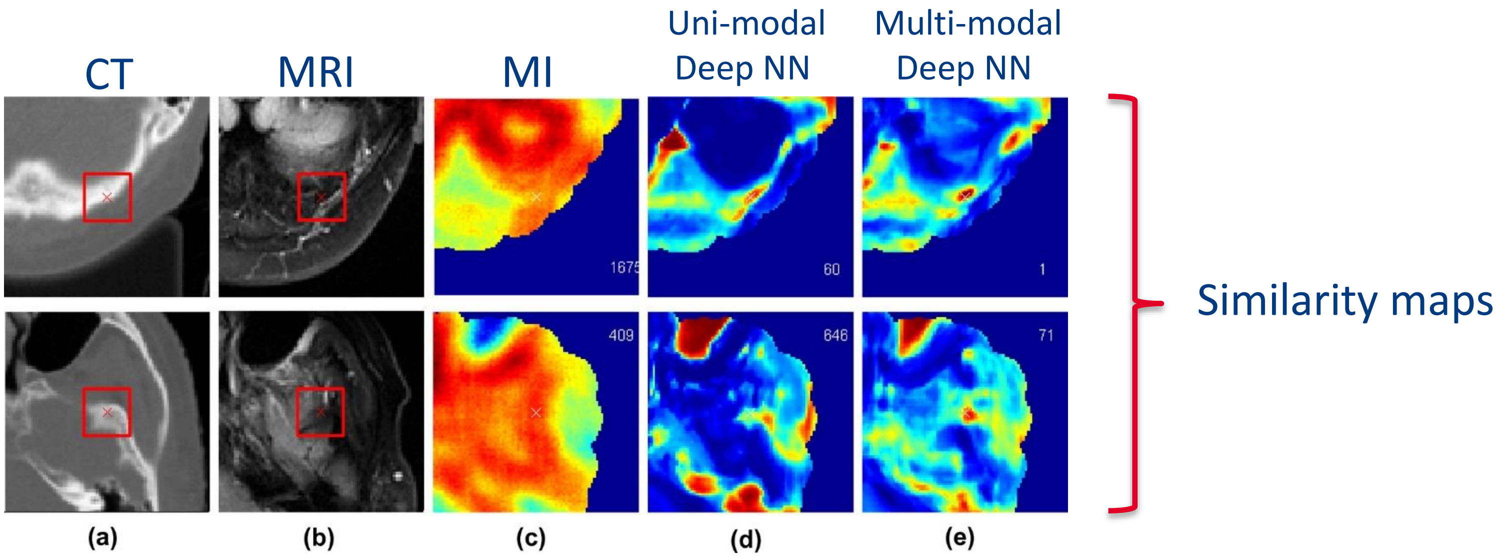
Haskins et al. (2019) Deep Learning in Medical Image Registration: A Survey. arXiv:1903.02026v1



A. Deep iterative registration

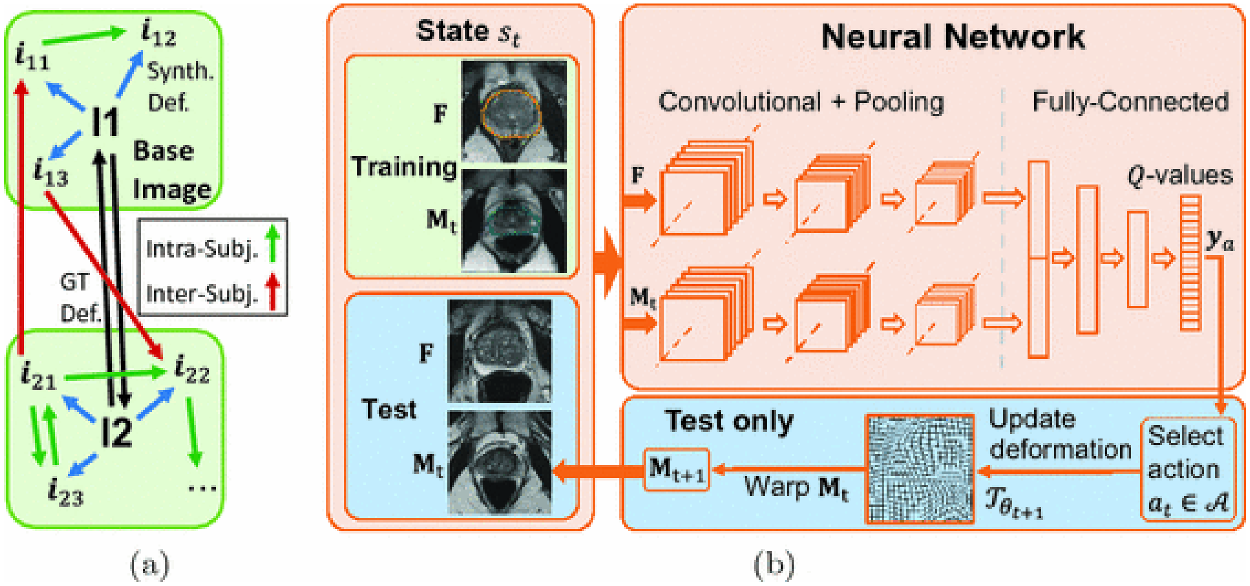
Use a classical registration method and learn one component

Example 1: *Learning multimodal feature extraction (Haskins et al., 2019)*

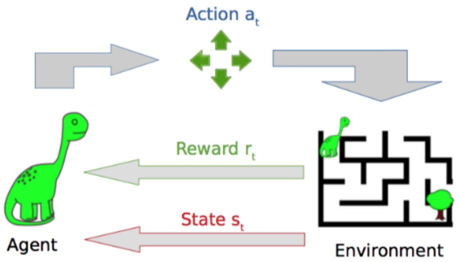


Haskins et al. (2019) Deep Learning in Medical Image Registration: A Survey. arXiv:1903.02026v1

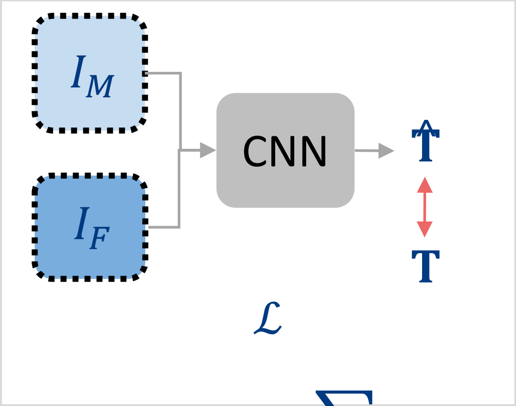
Example 2: *Reinforcement learning for image registration*



(a) Training Data Generation: **Synthetic deformations** (blue arrows) and inter-subject GT deformations (black) are used for intra- (green) and inter-subject (red) image pairs for training. (b) Dual-stream network used for Q-value prediction including complete single-stage Markov Decision Process for testing (blue background).



Krebs, Julian, et al. "Robust non-rigid registration through agent-based action learning." *International Conference on Medical Image Computing and Computer-Assisted Intervention*. Springer, Cham, 2017.

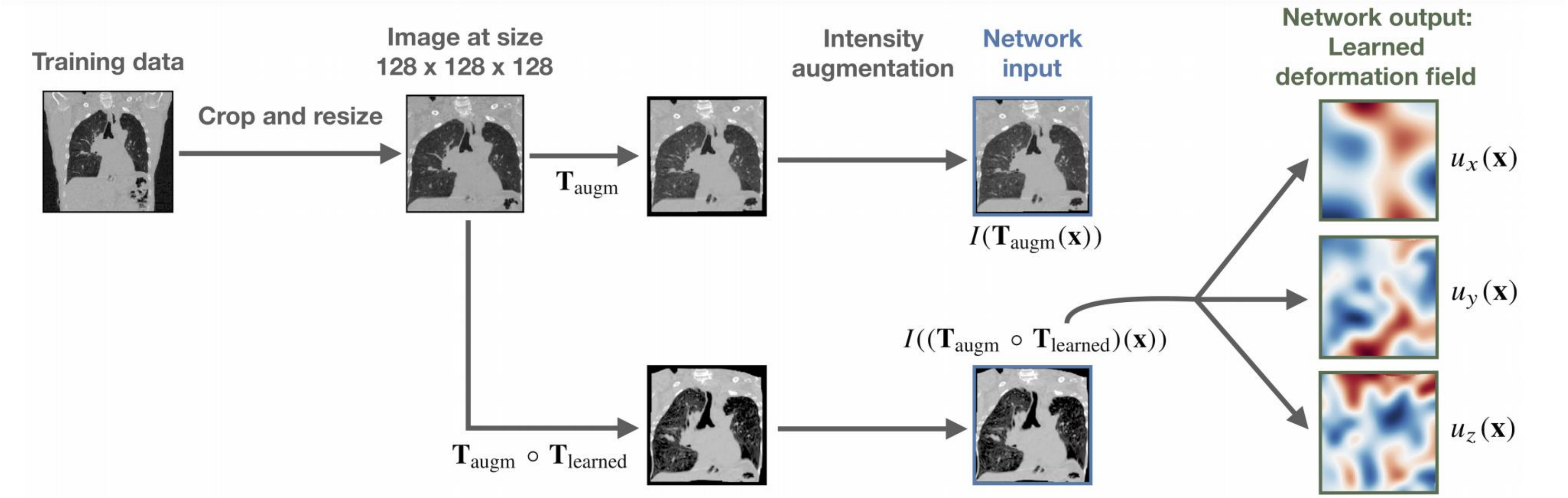


$$\mathcal{L} = \sum_{\mathbf{x}\in\Omega_F} \|\mathbf{T} - \hat{\mathbf{T}}\|$$

B. Supervised transformation estimation

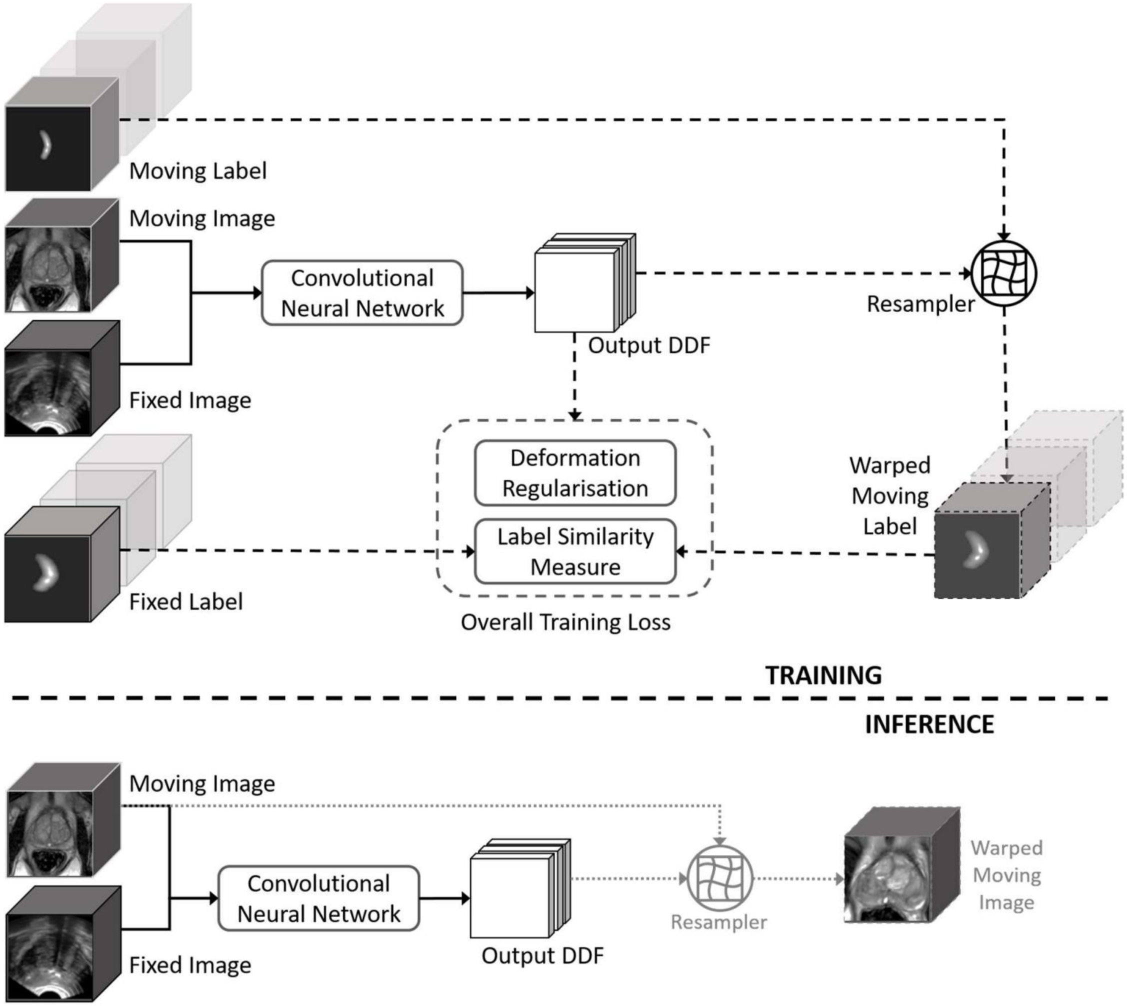
Requires many known transformations for training, use ground truth labels to calculate the loss

Example 1: *"On-the-fly" simulation of displacement fields: T_{augm} (Eppenhof & Pluim, 2018)*

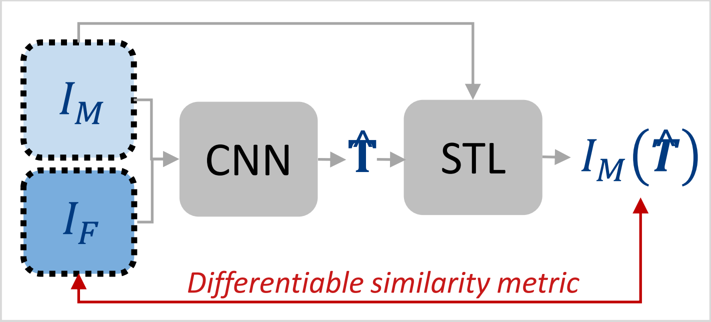


Eppenhof, Koen AJ, and Josien PW Pluim. "Pulmonary CT registration through supervised learning with convolutional neural networks." *IEEE transactions on medical imaging* 38.5 (2018): 1097-1105.

Example 2: *Weakly-supervised* CNN for MR-US registration



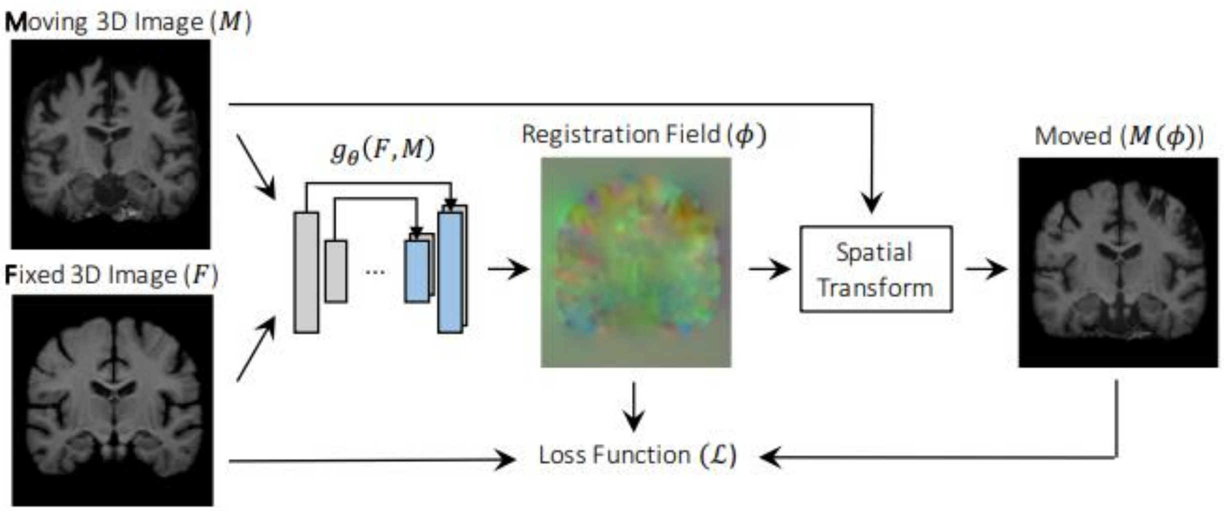
Hu, Yipeng, et al. "Weakly-supervised convolutional neural networks for multimodal image registration." *Medical image analysis* 49 (2018): 1-13.



C. Unsupervised transformation estimation

No ground truth needed, requires a differentiable similarity metric and a spatial transformer layer (STL).

Example 1: the *VoxelMorph framework (Balakrishnan et al., 2018)*

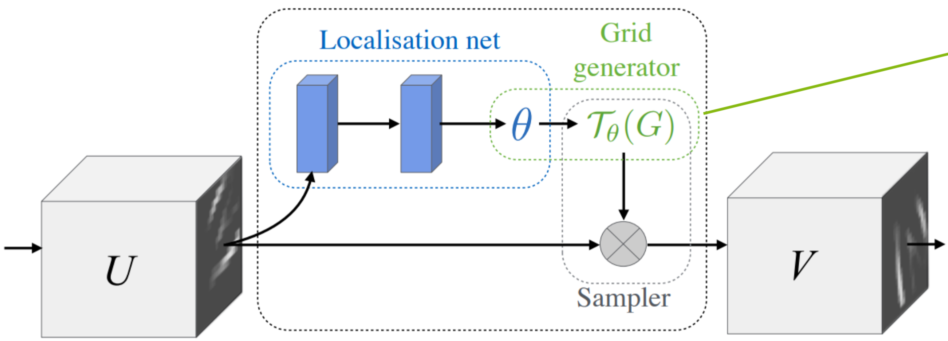


Balakrishnan et al. (2018): VoxelMorph: A Learning Framework for Deformable Medical Image Registration. arXiv:1909.05231v3

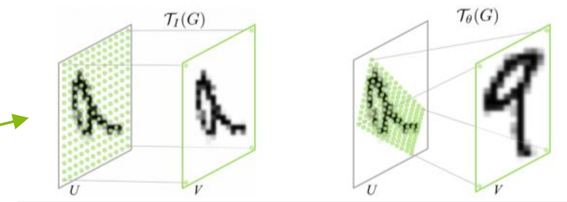
Spatial transformer networks (Jaderberg et al., NIPS 2015)

Spatial transformer = a learnable module that explicitly allows the spatial manipulation of data within the network

- *Differentiable*
- Can be inserted into existing convolutional neural networks
- Actively transforms feature maps (conditional on the feature map itself)



Spatial Transformer



Example $T_\theta(G)$ for an affine transformation:

$$\begin{pmatrix} x_i^s \\ y_i^s \end{pmatrix} = \mathcal{T}_\theta(G_i) = \mathtt{A}_\theta \begin{pmatrix} x_i^t \\ y_i^t \\ 1 \end{pmatrix} = \begin{bmatrix} \theta_{11} & \theta_{12} & \theta_{13} \\ \theta_{21} & \theta_{22} & \theta_{23} \end{bmatrix} \begin{pmatrix} x_i^t \\ y_i^t \\ 1 \end{pmatrix}$$

Jaderberg, Max, Karen Simonyan, and Andrew Zisserman. "Spatial transformer networks." *Advances in neural information processing systems*. 2015.

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Summary

- Parametric vs. non-parametric/deformable image registration
  - Displacement vector fields
- Different ways to use deep learning for image registration
  - Deep iterative registration
  - Supervised learning
  - Unsupervised learning
- Disadvantages of deep learning for image registration (performance, # of training data, ground truth, …)