IMAG/e

TU/e Technische Universiteit Eindhoven University of Technology

Deep learning for (deformable) 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:
  - Feedback on project 1
  - Question hour and example exam questions

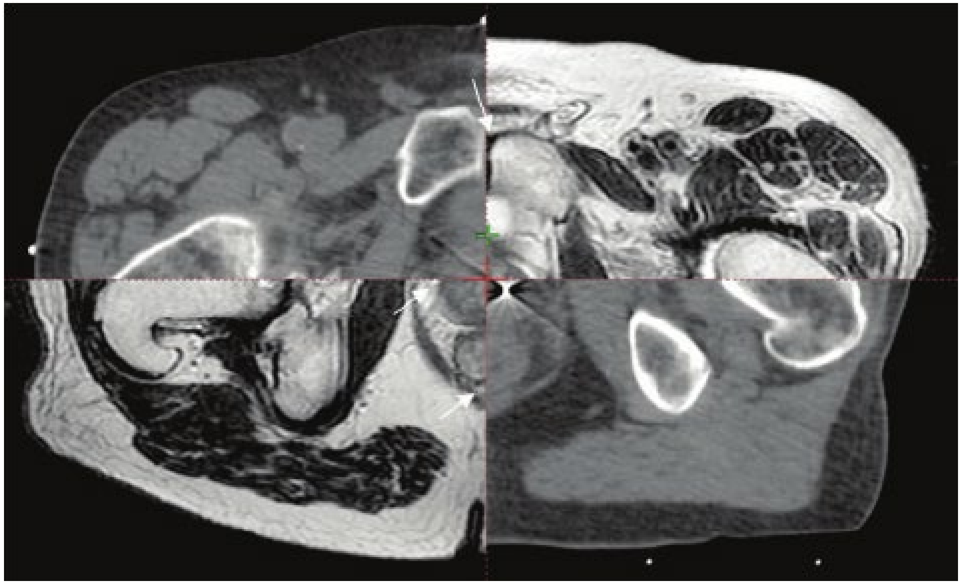
Medical image registration

Why important?

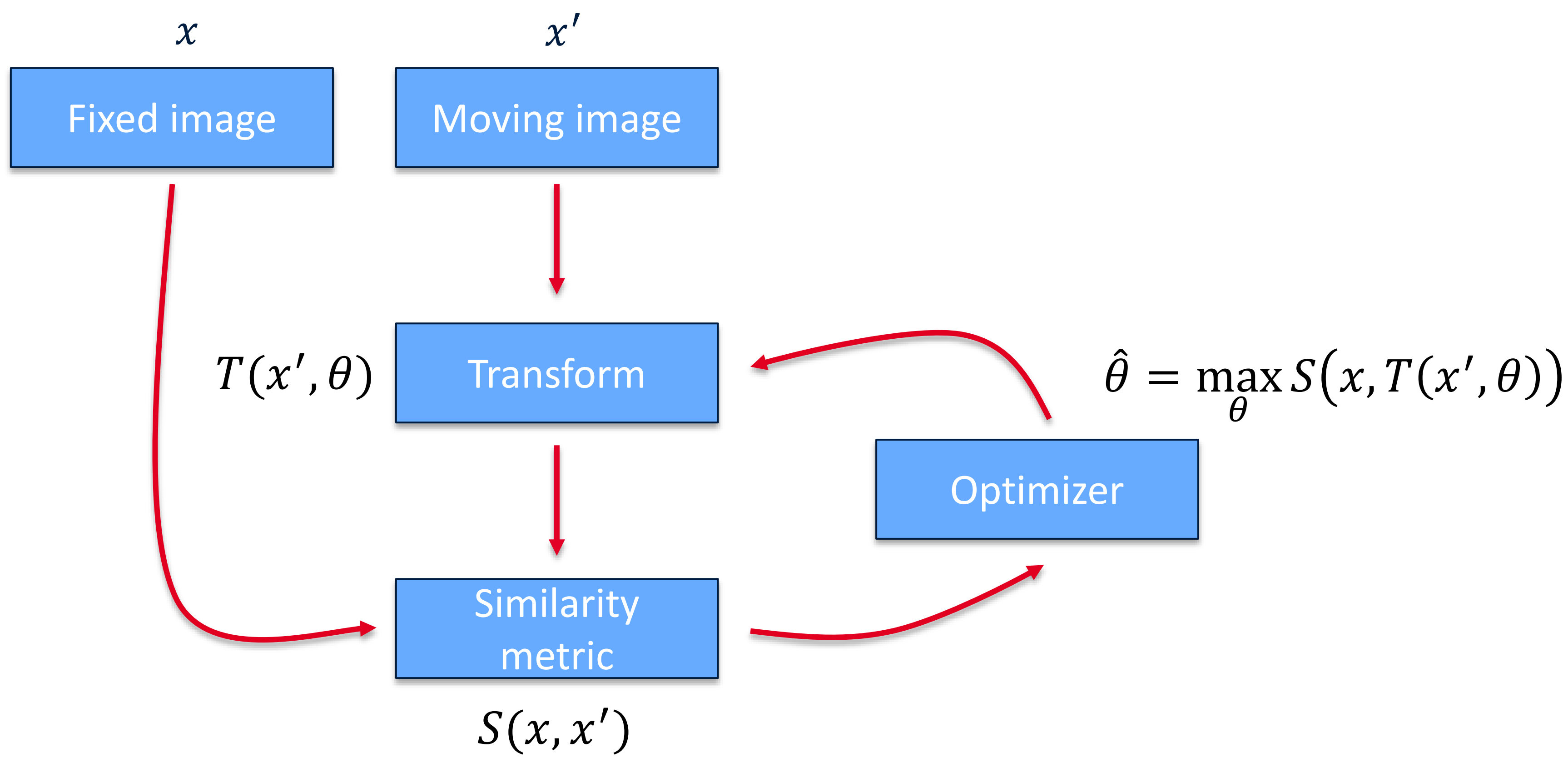
- Multi-modal registration (e.g. CT on MRI)
- Inter-subject (e.g. atlas registration)
- Longitudinal (e.g. treatment evaluation)

Remaining challenges:

- Large 3D volumes
- Accuracy vs. efficiency (speed)
- Intensity inhomogeneities and discontinuities
- Outlier rejection



Finding the optimal transformation



Rigid transformations

$$\mathbf{x}' = \mathbf{R}\mathbf{x} + \mathbf{t}$$

- Translation

$$\mathbf{t} = \begin{bmatrix} t_x \\ t_y \end{bmatrix}$$

- Rotation

$$\mathbf{R} = \begin{bmatrix} \cos(\phi) & -\sin(\phi) \\ \sin(\phi) & \cos(\phi) \end{bmatrix}$$

Affine transformations

$$\mathbf{x}' = \mathbf{A}\mathbf{x} + \mathbf{t}$$

Translation, rotations and:

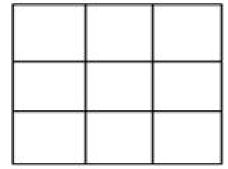
- Scaling

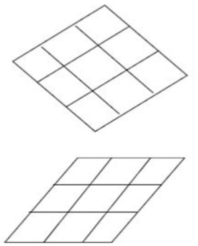
$$\mathbf{S} = \begin{bmatrix} s_x & 0 \\ 0 & s_y \end{bmatrix}$$

- Shearing

$$\mathbf{H} = \begin{bmatrix} 1 & h_x \\ h_y & 1 \end{bmatrix}$$

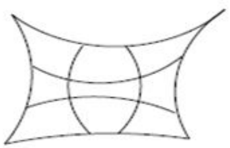
Transformation models





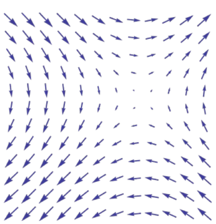
Rigid & Affine

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



Non-linear

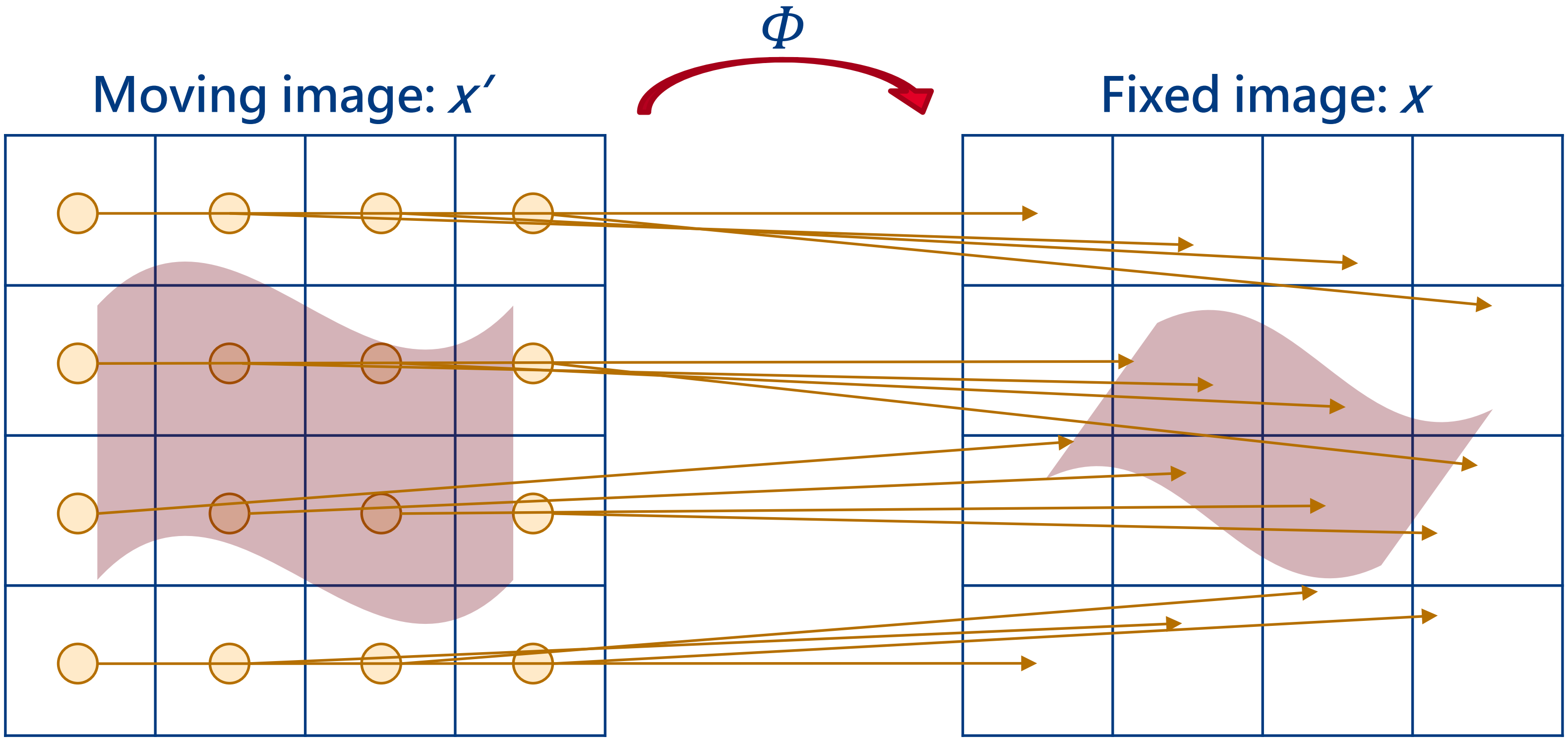
- Linear or higher order polynomials
- Spline-based

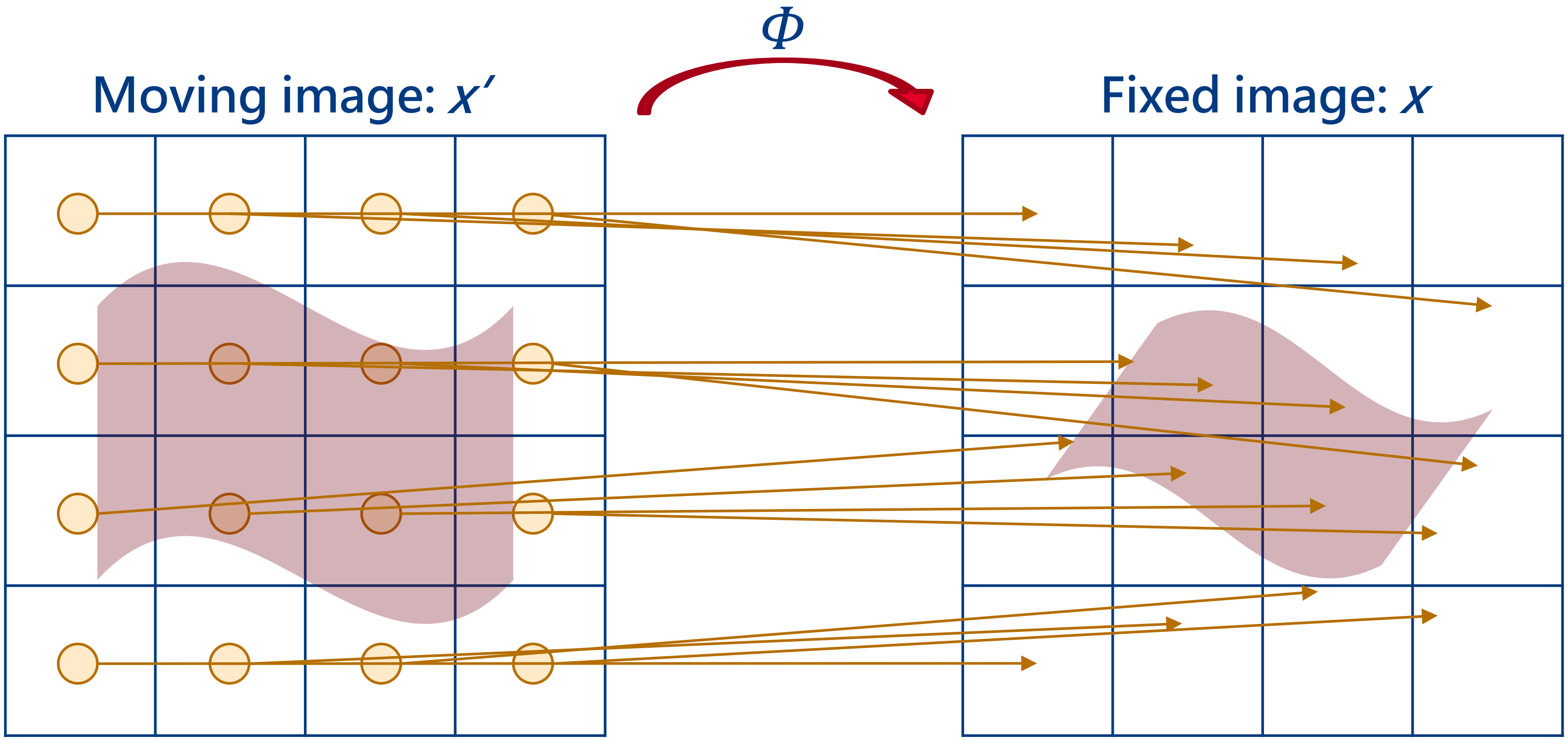


Non-parametric / deformable

- Allowing each image element to be displaced arbitrarily

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





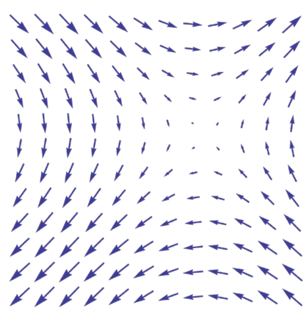
Deformation: $\varphi = \mathrm{Id} + u, \qquad \varphi : \Omega \rightarrow \mathbb{R}^d$

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

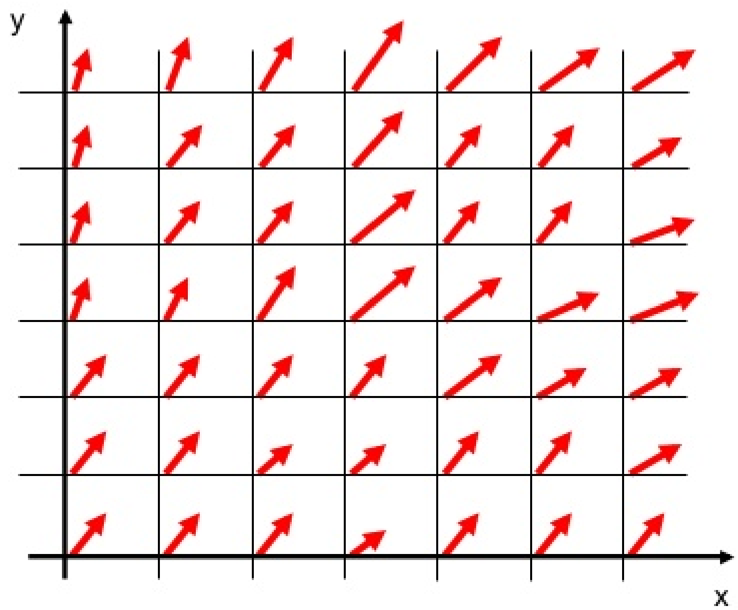
Displacement:

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

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. $1.5 \times 1.5 \times 4$ mm^3 voxels)

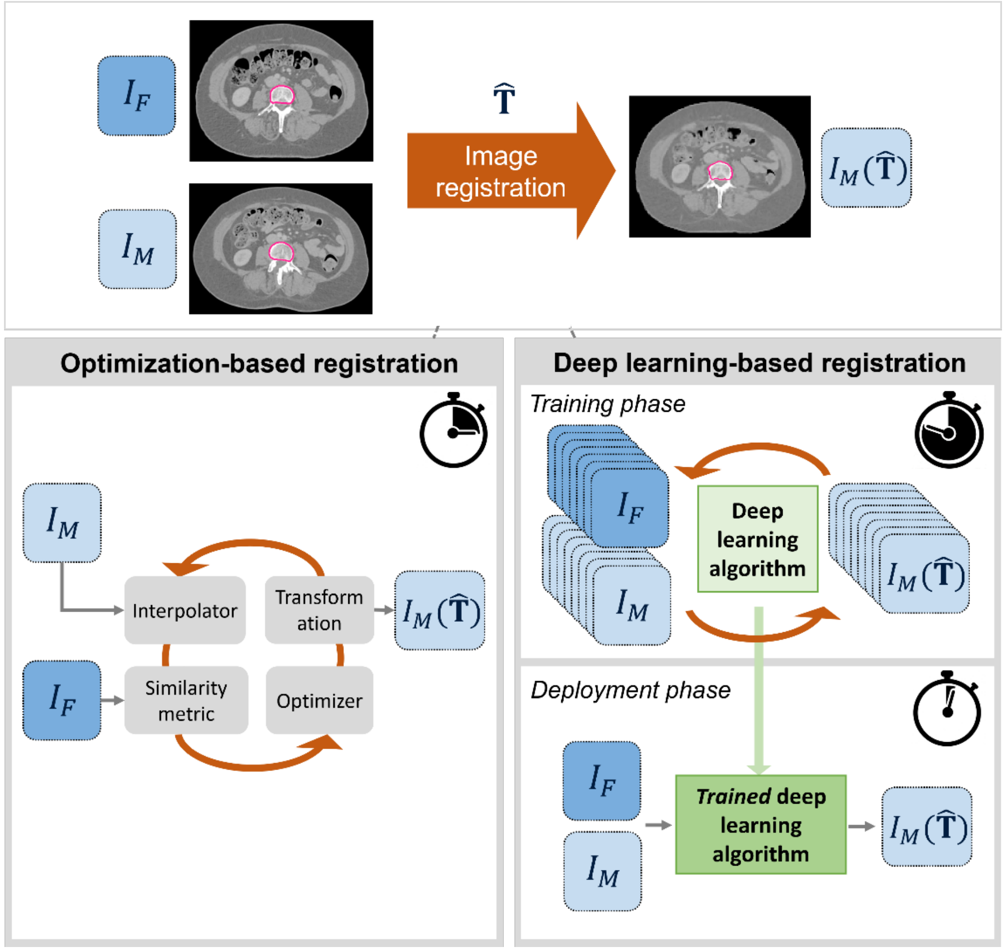
DOF = 3*Nx*Ny*Nz (!)

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.

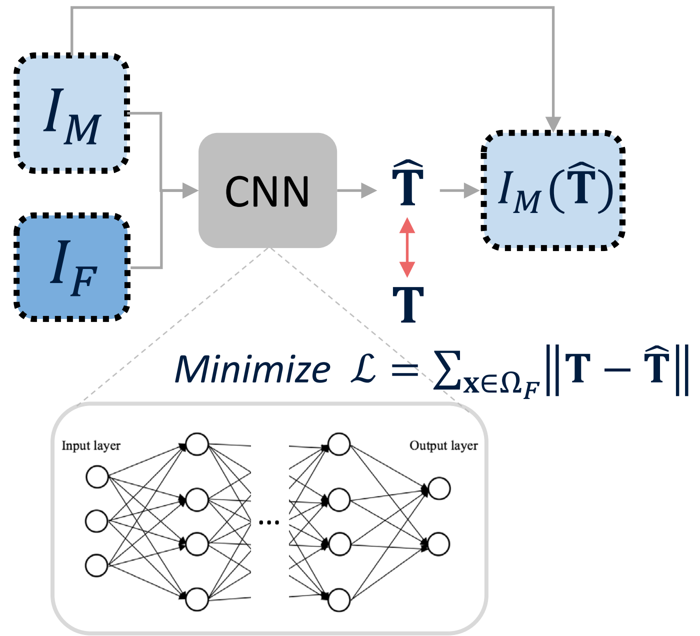
Why focus on deep learning for medical image registration?



Real time applications!

Learning image registration: how does it work?

Problem: how can we obtain the ground truth displacement $\mathbf{T}$?



A. Deep iterative registration

- Learn a component of a classical registration method

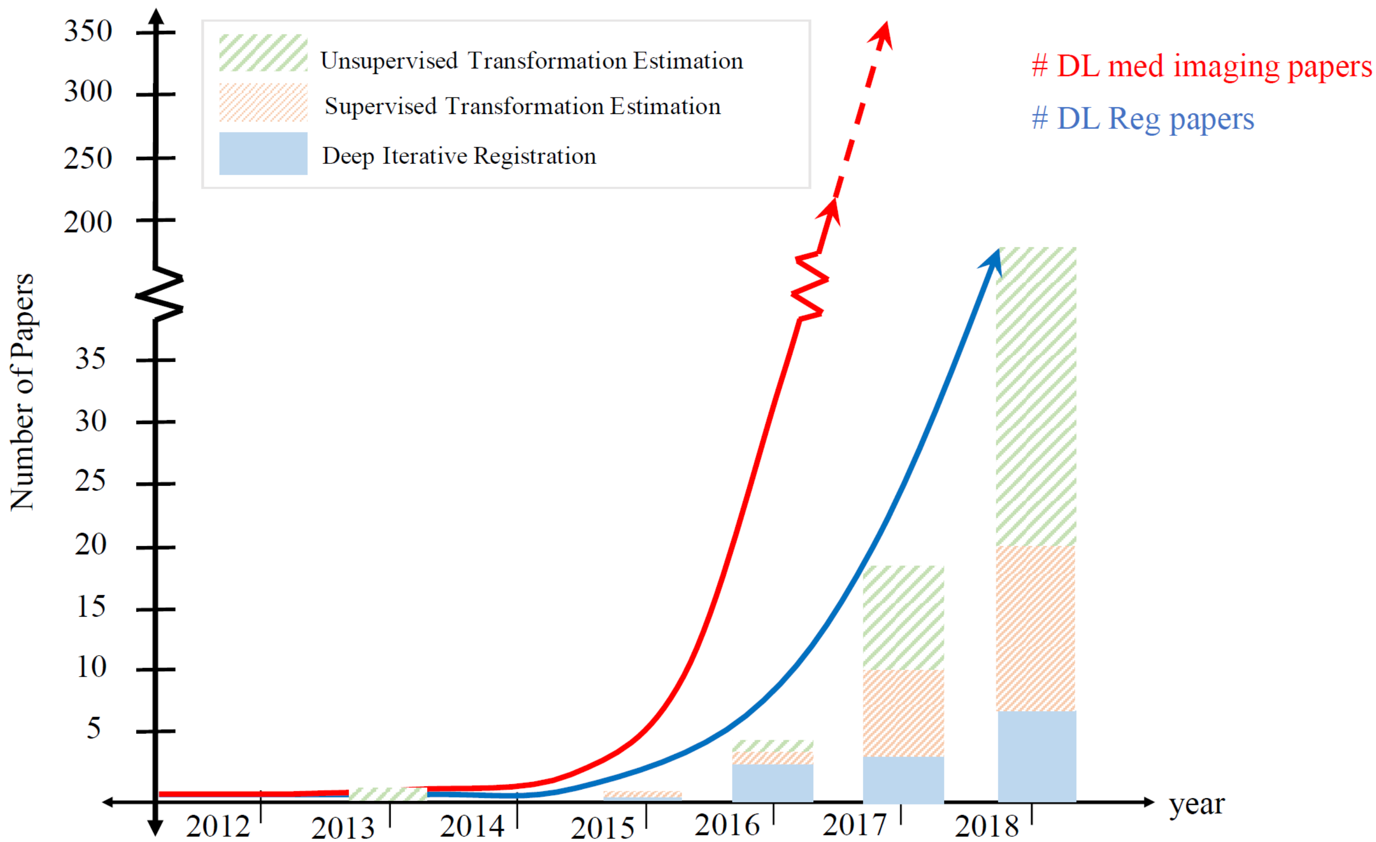
B. Supervised transformation estimation

- Obtain $\mathbf{T}$ using classical registration method
- or make synthetic ground truth

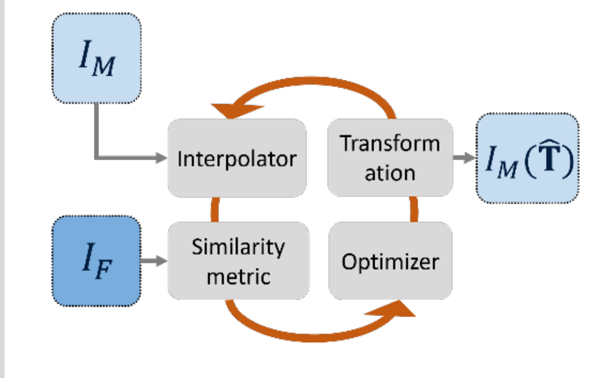
C. Unsupervised transformation estimation

- Use similarity metric to judge $I_M(\hat{\mathbf{T}})$

Publications on deep learning for medical image registration



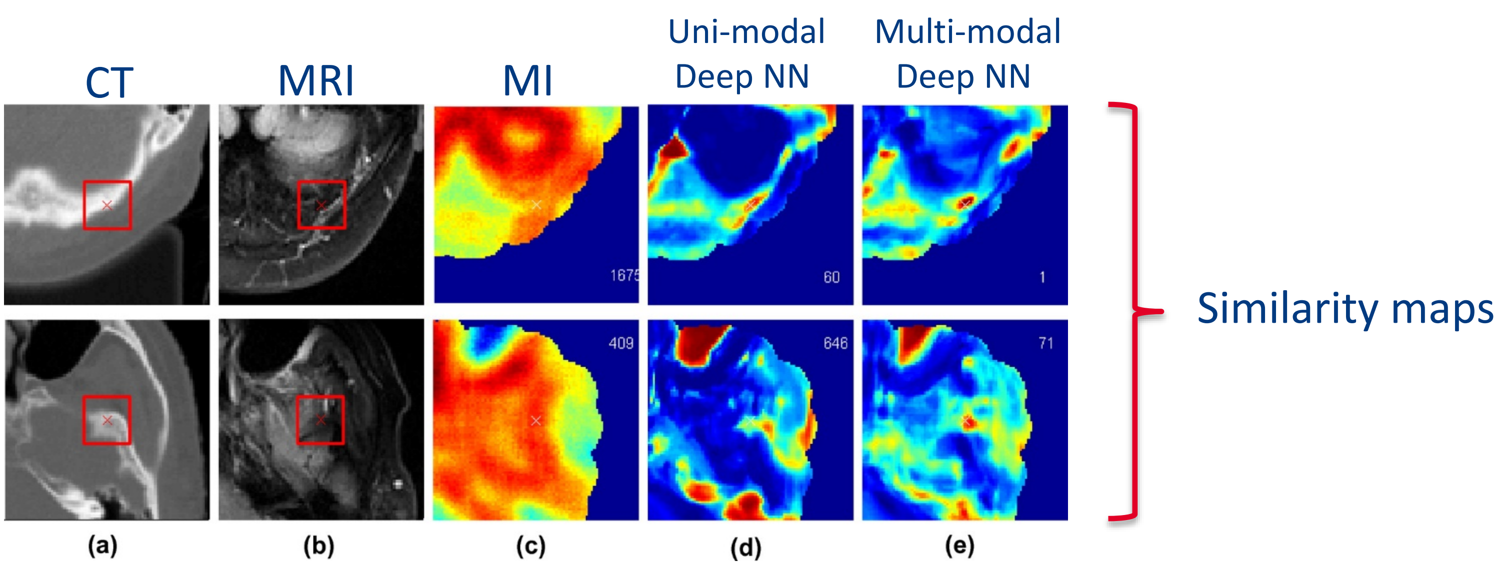
Haskins et al. (2019) Deep Learning in Medical Image Registration: A Survey. arXiv:1903.02026v1



A. Deep iterative registration

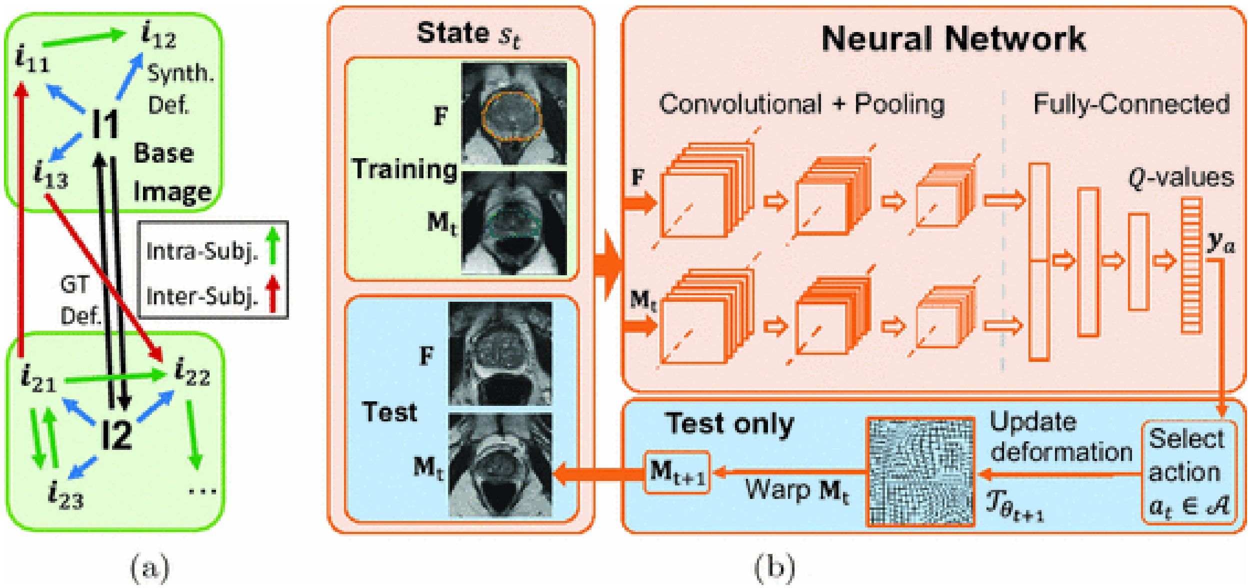
Use a classical registration method and learn one component

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

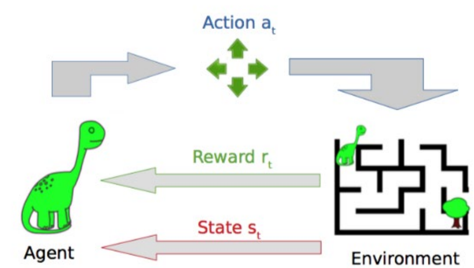


Haskins et al. (2019) Deep Learning in Medical Image Registration: A Survey. arXiv:1903.02026v1

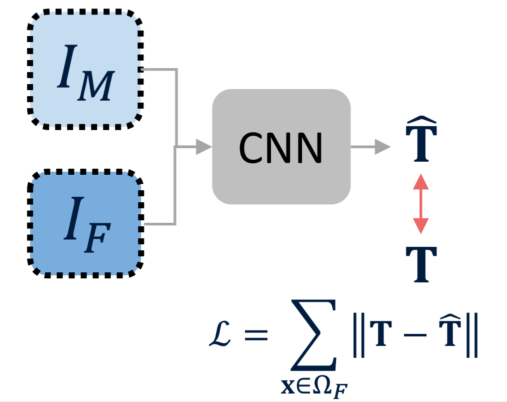
Example 2: *Reinforcement learning for image registration*



(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).



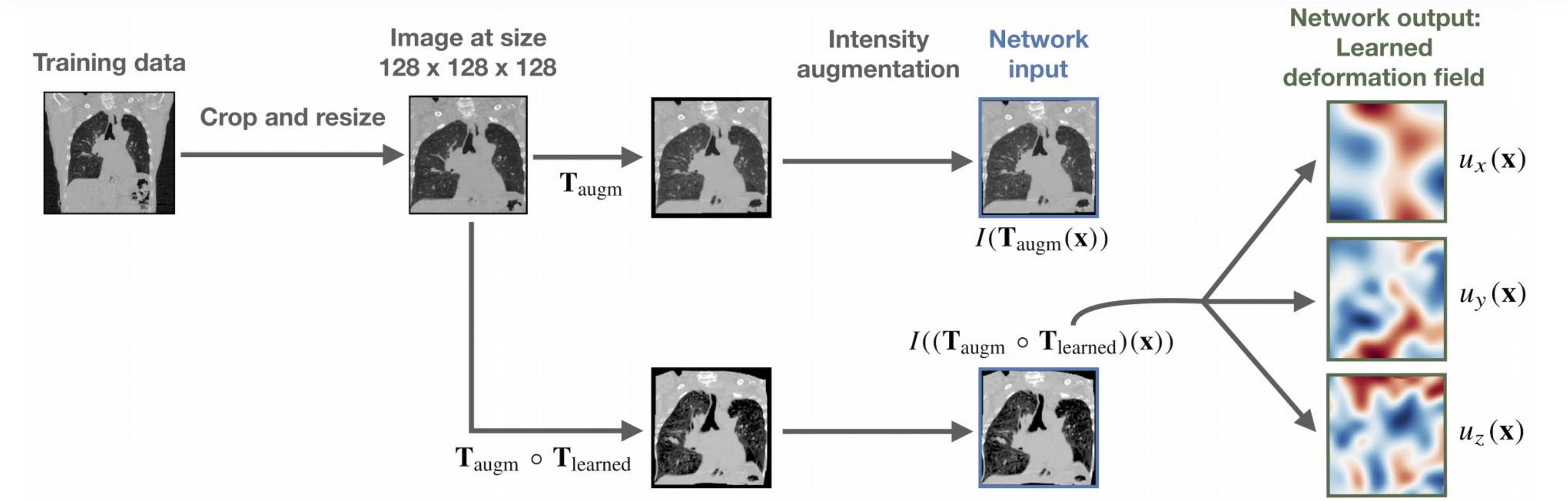
Krebs, Julian, et al. "Robust non-rigid registration through agent-based action learning." *International Conference on Medical Image Computing and Computer-Assisted Intervention*. Springer, Cham, 2017.



B. Supervised transformation estimation

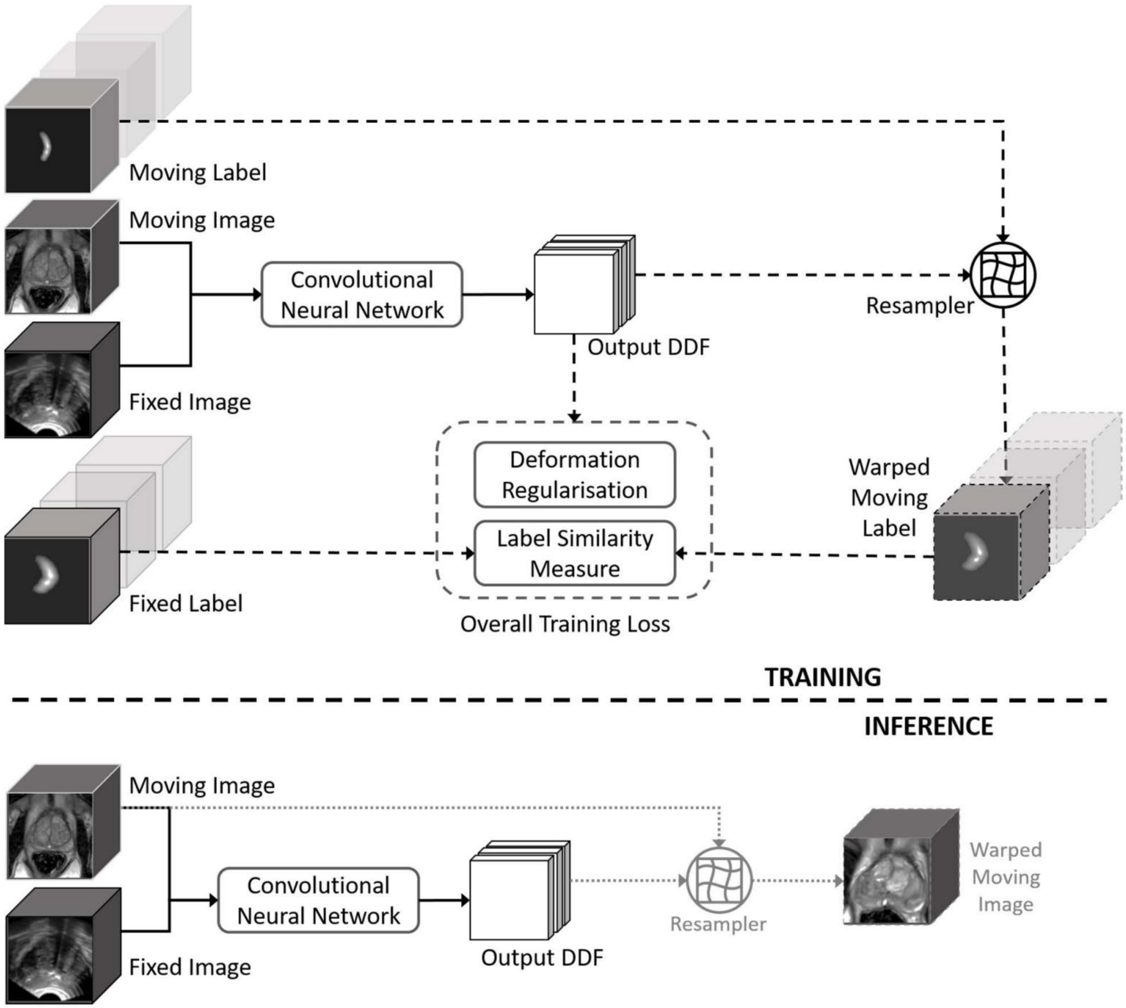
Requires many known transformations for training, use ground truth labels to calculate the loss

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

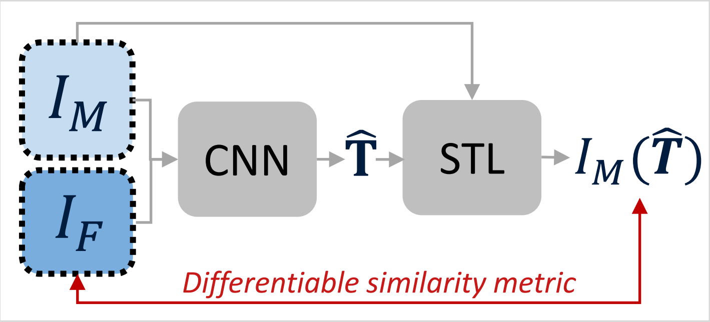


Eppenhof, Koen AJ, and Josien PW Pluim. "Pulmonary CT registration through supervised learning with convolutional neural networks." *IEEE transactions on medical imaging* 38.5 (2018): 1097-1105.

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



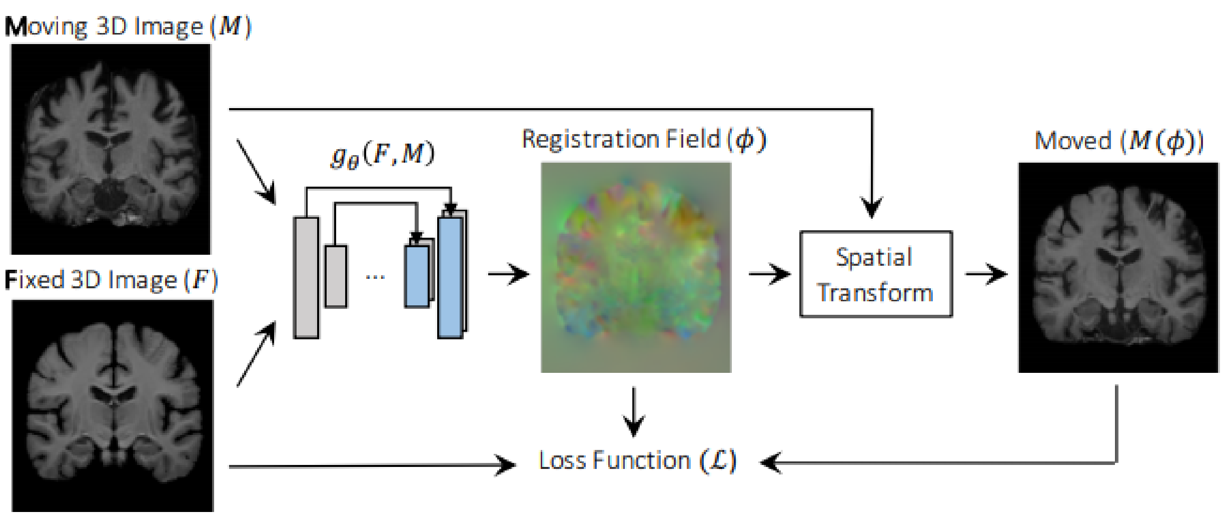
Hu, Yipeng, et al. "Weakly-supervised convolutional neural networks for multimodal image registration." *Medical image analysis* 49 (2018): 1-13.



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)*

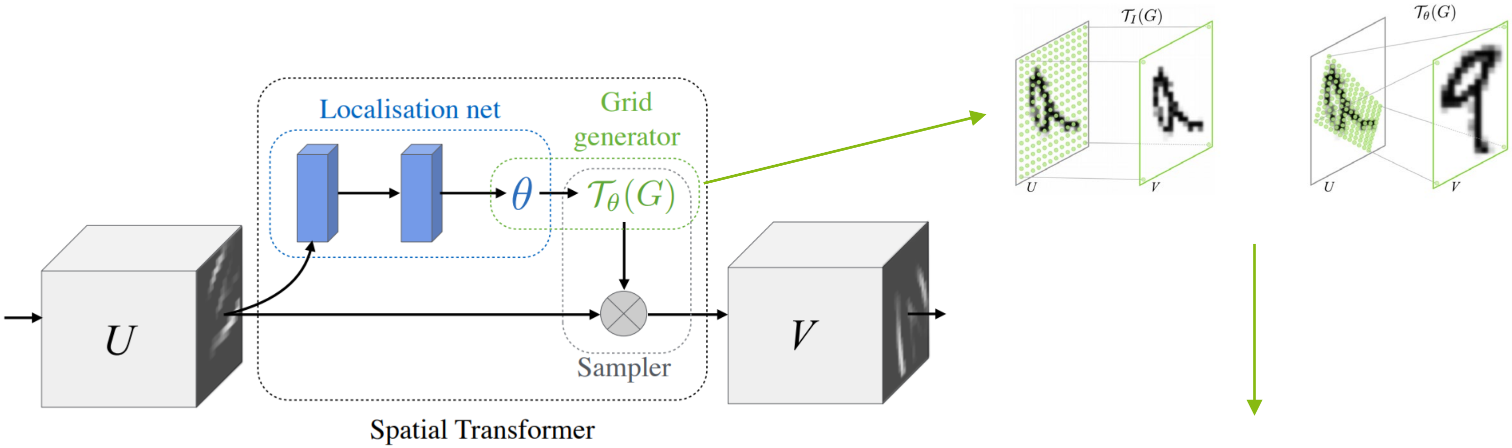


Balakrishnan et al. (2018): VoxelMorph: A Learning Framework for Deformable Medical Image Registration. arXiv:1909.05231v3

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)

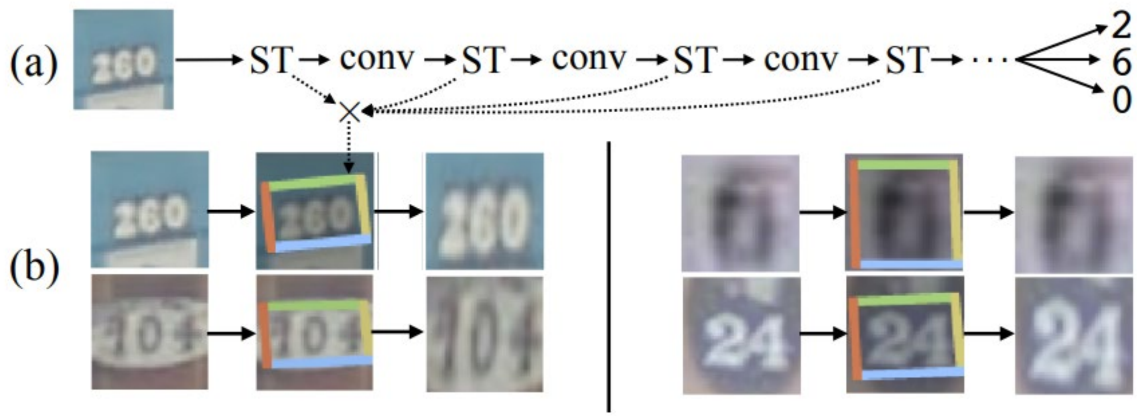


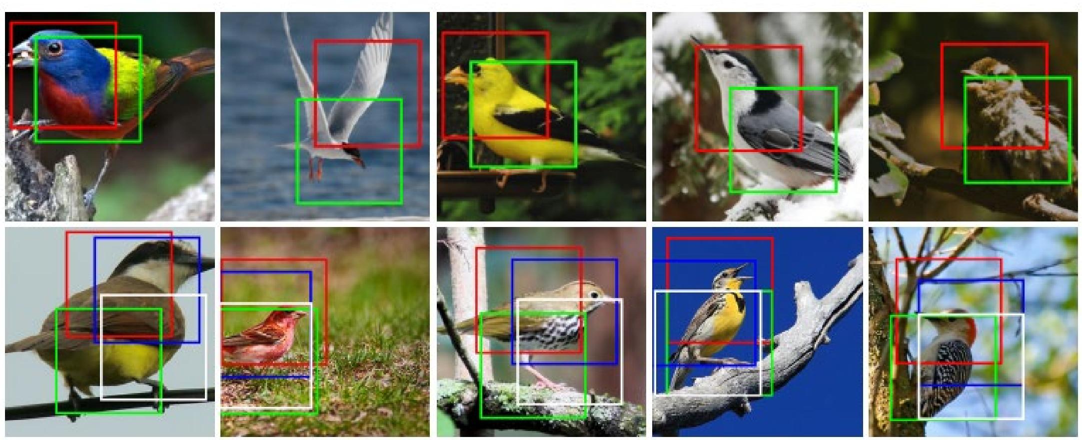
Example $T_\theta(G)$ for an affine transformation:

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

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

CNNs are in essence not invariant to translation, scale, rotation and more generic warping of the input data





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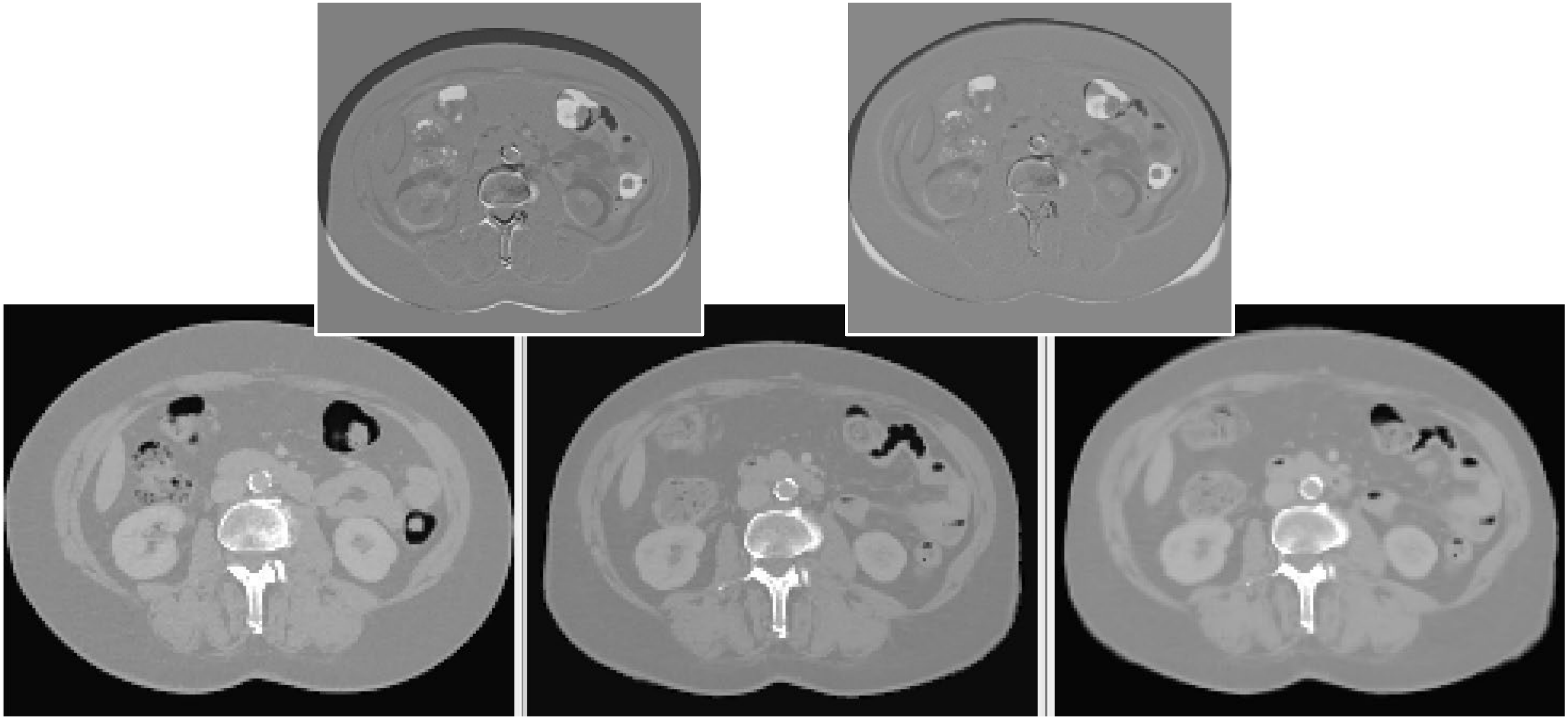
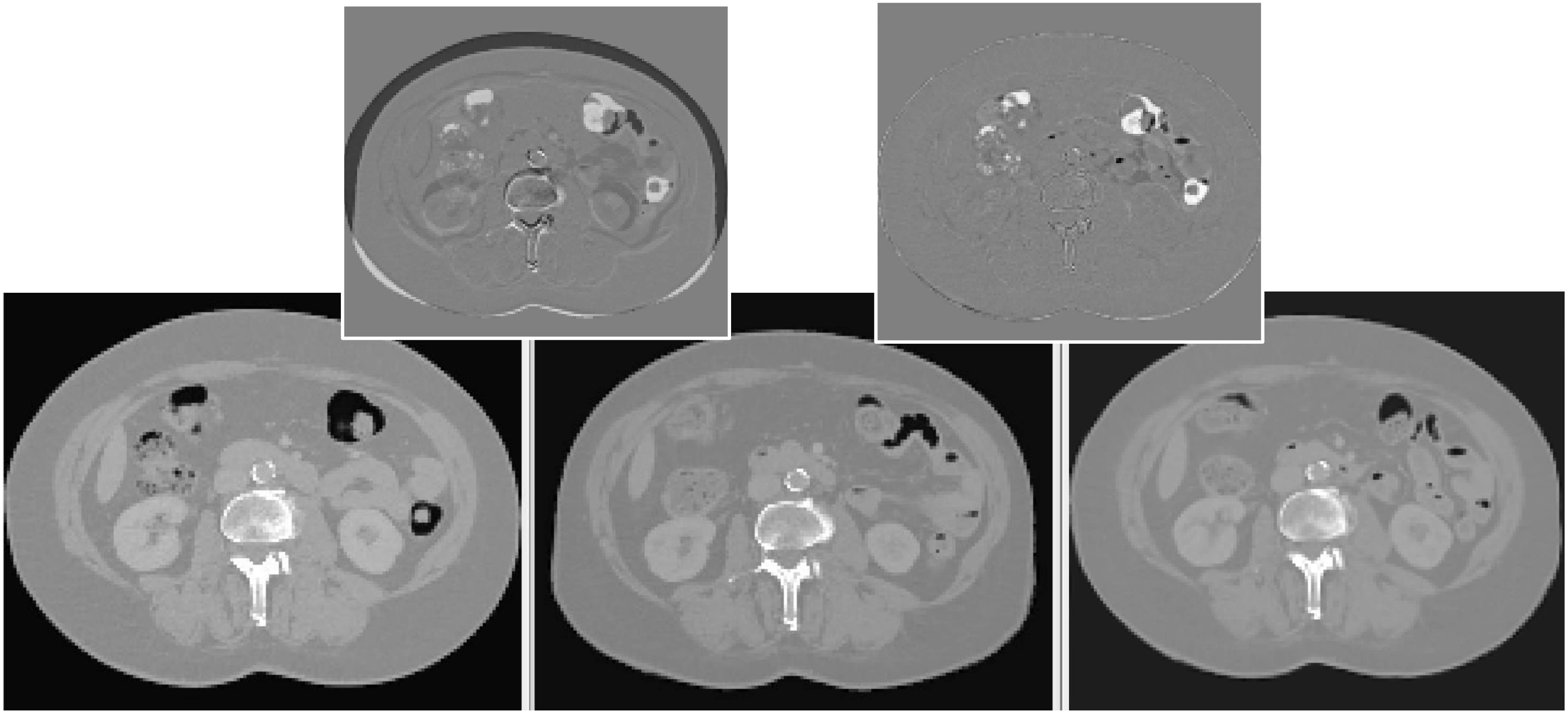
Example of my own experiments: **VoxelMorph**



Fixed Moving Voxelmorph registration

Example of my own experiments: the **NiftyReg** toolbox (non-deep learning-based, slow but accurate)



Fixed Moving NiftyReg registration

NiftyReg: an open-source software for efficient medical image registration (http://cmictig.cs.ucl.ac.uk/wiki/index.php/NiftyReg

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, …)

Feedback Project 1

General feedback Project 1

- **Results**: make sure to organize the results well, logical order, caption for each figure!
- **Discussion**: do the discussed topics directly follow from the results?
- **Use references**! (NB: scientific writing)
- **Reproducibility**: e.g. create a notebook that allows others to easily repeat the experiment or run the code

Grades and group-specific feedback have been communicated with all groups via Canvas, if have questions about this, ask your TA (or me).

Preparing for the exam

How can I prepare for the exam?

- (Re)study all exercises (NB: open questions)
  - Answers on Canvas (soon)
- Questions in the lecture slides
- Group exercises lecture 2 by Navchetan (“Deep learning frameworks & applications”)
- Practice exam

Example exam questions: registration case studies

7. Case 1: Neuronavigation

The neurosurgery department recently acquired a new neuronavigation system with a probe (Figure 2) that is depicted on the computer screen showing the MRI scan of the patient. The system relies on a registration between N extrinsic fiducials depicted on the MRI scan and the physical fiducials.

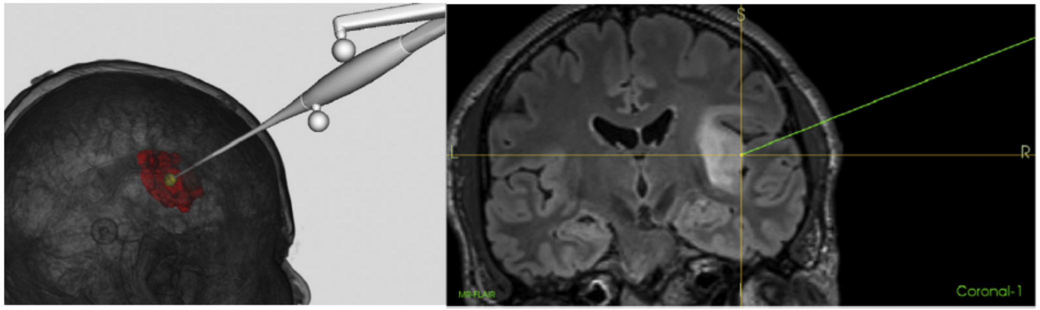


Figure 2: Three-dimensional rendering of the preoperative MRI scan and the probe (left), and a coronal slice of the MRI scan (right).

A nice feature of the navigation system is that it allows the neurosurgeon to check the accuracy of the registration by touching some points of the patient's anatomy with the probe, after which the system calculates an estimate of the registration error. Halfway through the first surgery, the neurosurgeon wants to perform a "sanity check" of the registration and touches all N fiducials with the probe. The surgeon then decides to omit the fiducial with the largest error and repeats the registration based on the remaining $N - 1$ fiducials.

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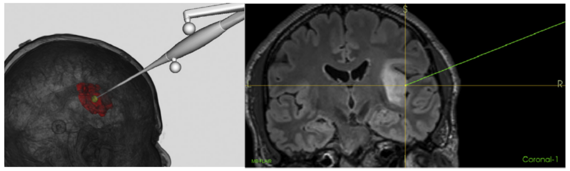

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1. What type of registration problem is this?
   (a) Uni-modal
   (b) Multi-modal
   (c) Longitudinal
   (d) Atlas-based
   (e) None of the above

2. Which transformation model is required?
   (a) Deformable
   (b) Affine
   (c) Rigid
   (d) Non-linear

3. Which image similarity metric is used for the registration?
   (a) Sum of square differences
   (b) (Normalized) cross-correlation
   (c) Mutual information
   (d) None of the above

4. How can you find the optimal transformation?
   (a) Gradient ascent
   (b) Gradient descent
   (c) Use reinforcement learning
   (d) Solve the orthogonal Procrustes problem
   (e) Solve $X'X^T(XX^T)^{-1}$

5. Which metric should be used to evaluate the registration performance?
   (a) Sensitivity
   (b) Dice similarity coefficient (DSC)
   (c) Target registration error (TRE)
   (d) Accuracy
   (e) Hausdorff distance
   (f) Specificity

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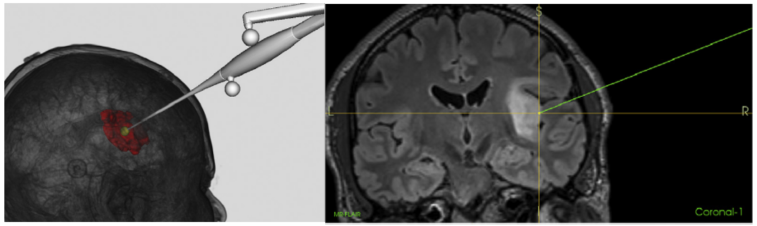

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(b) (4 points) *Open question (max. 100 words)*: Explain what will happen with the fiducial registration error (FRE) and the target registration error (TRE) after dropping this fiducial. What do you think of this sanity check and the effect on the accuracy of the navigation system?

8. Case 2: Adaptive radiotherapy

You are doing an internship at the Radiotherapy department of the UMC Utrecht, where you are asked to develop a new image registration algorithm to treat patients with prostate cancer on the MR-linac. The goal is to use daily MR images of the abdominopelvic area to adjust the radiation treatment plan for daily anatomical changes with respect to the planning CT. You have access to the planning CT and daily MR images of 100 patients, with organ delineations of the bladder, prostate (= clinical target volume), pelvis and rectum (Figure 3). Note that the abdominopelvic area is known for many local changes in anatomy that can occur due to bowel movements, bladder filling etc.

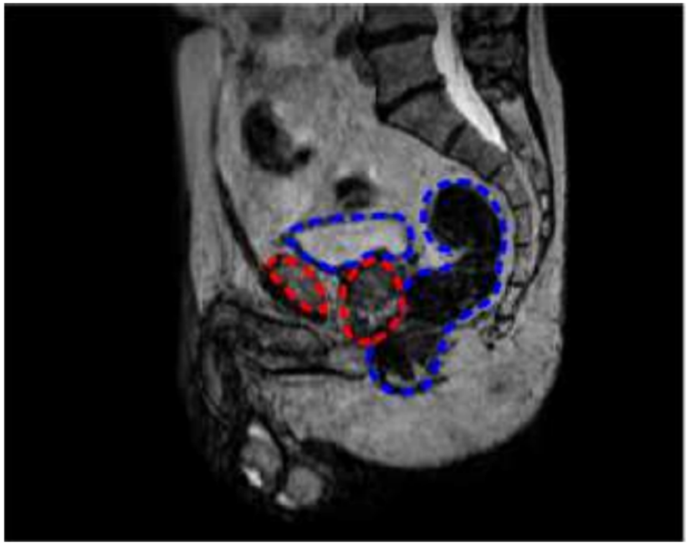

Figure 3: Example of an abdominopelvic MR image. Red dashed lines enclose the anatomical structures that are considered to be incompressible (prostate and pelvis), whereas the blue dashed lines indicate the compressible structures (bladder and rectum). Image courtesy of Zachiu et al. (2020).

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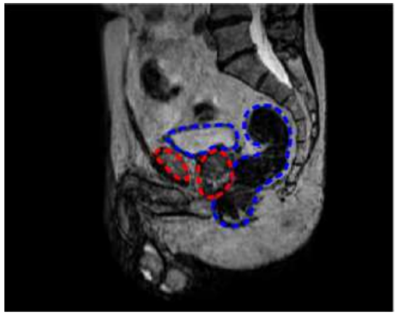

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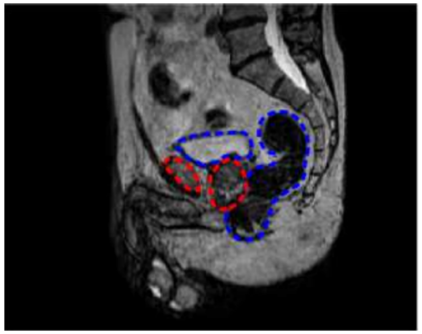

(b) (4 points) *Open question (max. 100 words)*: Describe an imaginary image registration algorithm to solve this challenging registration task. You may want to consider the following questions:

- What type of image registration algorithm would you aim for, and why?
- What are the most important technical and clinical requirements to consider (e.g. in terms of computational time and accuracy)?
- How could you validate your algorithm?