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Specimen SPECT for Intra-operative **A**ssistance in Radio-guided **S**urgery

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Technische Universität München

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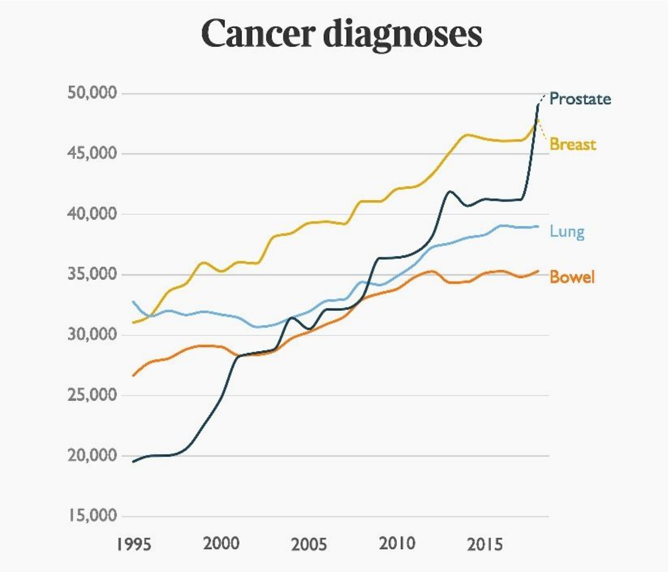
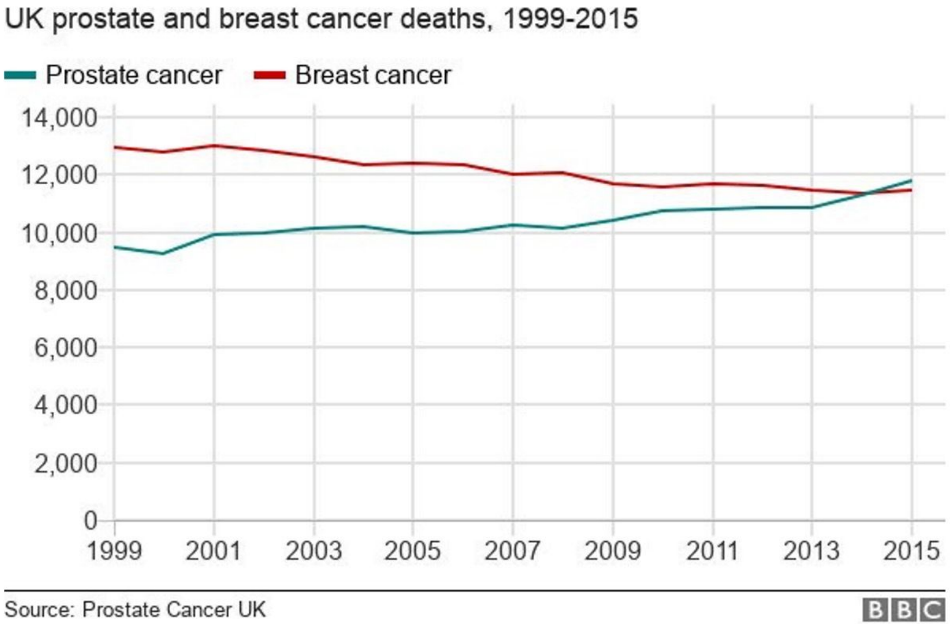
Introduction

- **Prostate cancer** is the 4th most common cancer overall and the 2nd most commonly occurring cancer in men. [1]
- The count of prostate cancer patients surpasses other deadliest cancer types since 2014. [2]



Source: Prof. Christopher Eden, Refer [x]



[1] Prostate cancer statistics 2020, *World Cancer Research Fund International*, accessed 19 February 2023, <https://www.wcrf.org/cancer-trends/prostate-cancer-statistics> .
[2] SANTIS Clinic Website > Prostate Cancer Information Centre.Testing & Diagnosis> The importance of celebrities in increasing the awareness of prostate cancer, accessed 27.02.2023, <https://www.santishealth.org/prostate-cancer-information-centre/the-importance-of-celebrities-in-increasing-the-awareness-of-prostate-cancer/>.

Introduction

- General treatment: **Radical Prostatectomy** (removal of entire prostate cancer tissue). [3]

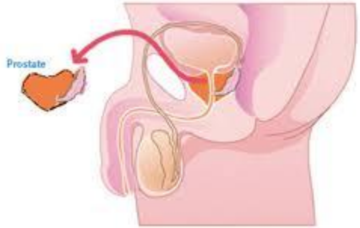


Figure 1: Prostate tissue

- Confirmation of **“resection margin”** is required during surgery. [3]

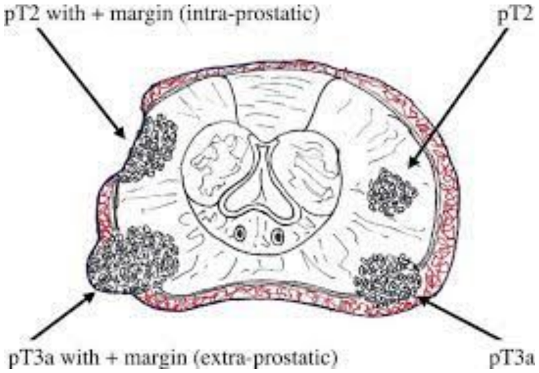


Figure 2: Resection Margin

[3] Montironi R, van der Kwast T, Boccon-Gibod L, Bono AV, Boccon-Gibod L. Handling and pathology reporting of radical prostatectomy specimens. Eur Urol. 2003 Dec;44(6):626-36. doi: 10.1016/s0302-2838(03)00381-6. PMID: 14644113.

Motivation / Problem statement

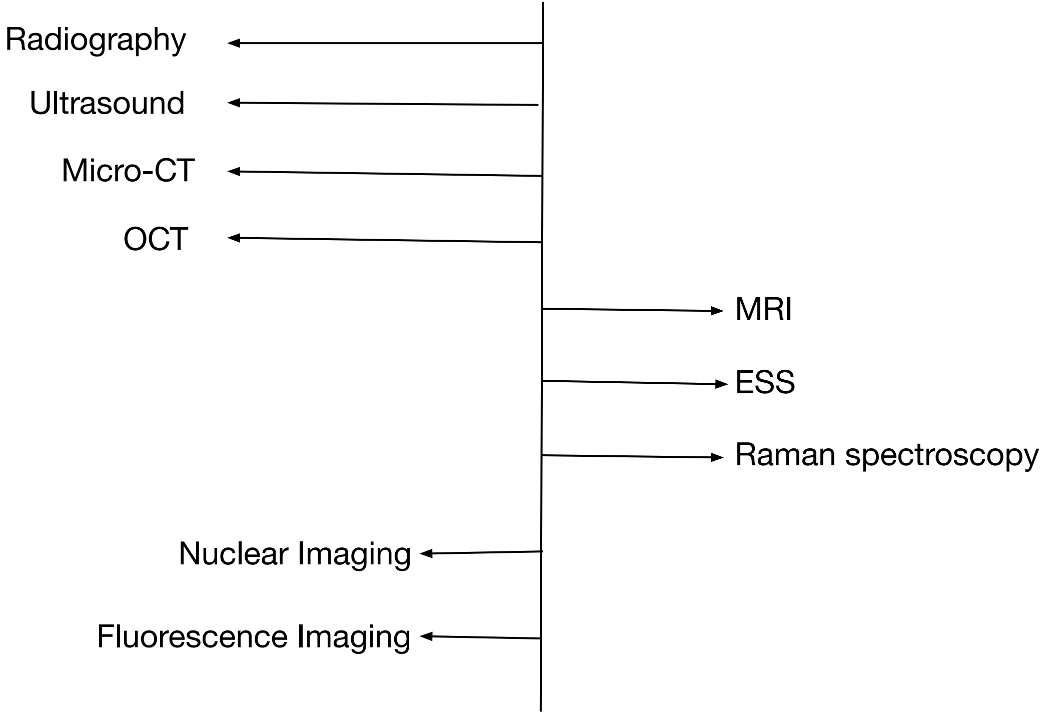
- Problem 1: Requirement of a Pathologist in the OR. [3]
- Problem 2: Time consuming for sample preparation. [4]
- Problem 3: Prostate tissue undergoes faster autolysis than most of the other organs. [5]

[3] Montironi R, van der Kwast T, Boccon-Gibod L, Bono AV, Boccon-Gibod L. Handling and pathology reporting of radical prostatectomy specimens. Eur Urol. 2003 Dec;44(6):626-36. doi: 10.1016/s0302-2838(03)00381-6. PMID: 14644113.

[4] Jorns JM, Visscher D, Sabel M, Breslin T, Healy P, Daignaut S, Myers JL, Wu AJ. Intraoperative frozen section analysis of margins in breast conserving surgery significantly decreases reoperative rates: one-year experience at an ambulatory surgical center. Am J Clin Pathol. 2012 Nov;138(5):657-69. doi: 10.1309/AJCP4IEMXCJ1GDTS. PMID: 23086766; PMCID: PMC3988579.

[5] Montironi R, Lopez Beltran A, Mazzucchelli R, Cheng L, Scarpelli M. Handling of radical prostatectomy specimens: total embedding with large-format histology. Int J Breast Cancer. 2012;2012:932784. doi: 10.1155/2012/932784. Epub 2012 Jul 10. PMID: 22844601; PMCID: PMC3400332.

Relevant research works on resection margin imaging



[CT: Computed Tomography; OCT: Optical Coherence Tomography; MRI: Magnetic Resonance Imaging; ESS: Elastic Scattering Spectroscopy]

[6] Heidkamp J, Scholte M, Rosman C, Manohar S, Fütterer JJ, Rovers MM. Novel imaging techniques for intraoperative margin assessment in surgical oncology: A systematic review. Int J Cancer. 2021 Aug 1;149(3):635-645. doi: 10.1002/ijc.33570. Epub 2021 May 4. PMID: 33739453; PMCID: PMC8252509.

Relevant research works on resection margin imaging

Low diagnostic accuracy!

- Radiography
- Ultrasound
- Micro-CT
- OCT

- MRI
- ESS
- Raman spectroscopy

- Nuclear Imaging
- Fluorescence Imaging

[CT: Computed Tomography; OCT: Optical Coherence Tomography; MRI: Magnetic Resonance Imaging; ESS: Elastic Scattering Spectroscopy]

[6] Heidkamp J, Scholte M, Rosman C, Manohar S, Fütterer JJ, Rovers MM. Novel imaging techniques for intraoperative margin assessment in surgical oncology: A systematic review. Int J Cancer. 2021 Aug 1;149(3):635-645. doi: 10.1002/ijc.33570. Epub 2021 May 4. PMID: 33739453; PMCID: PMC8252509.

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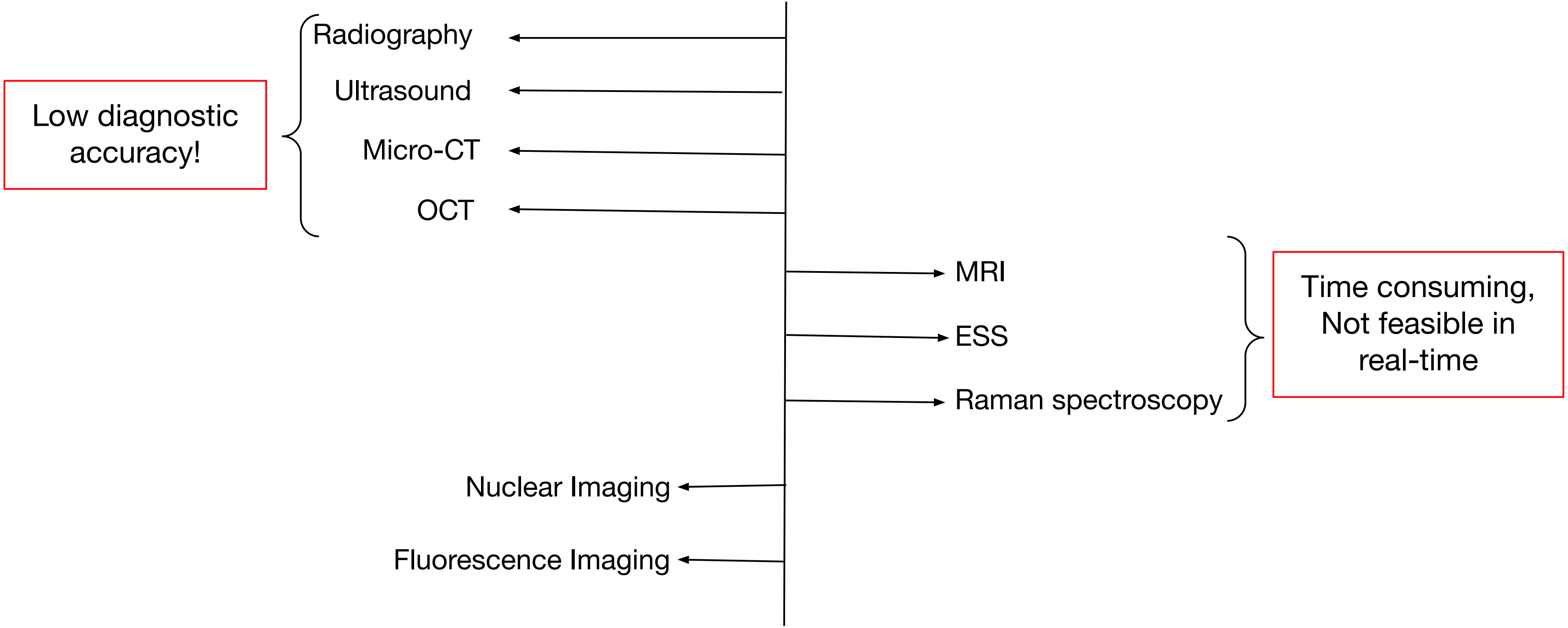

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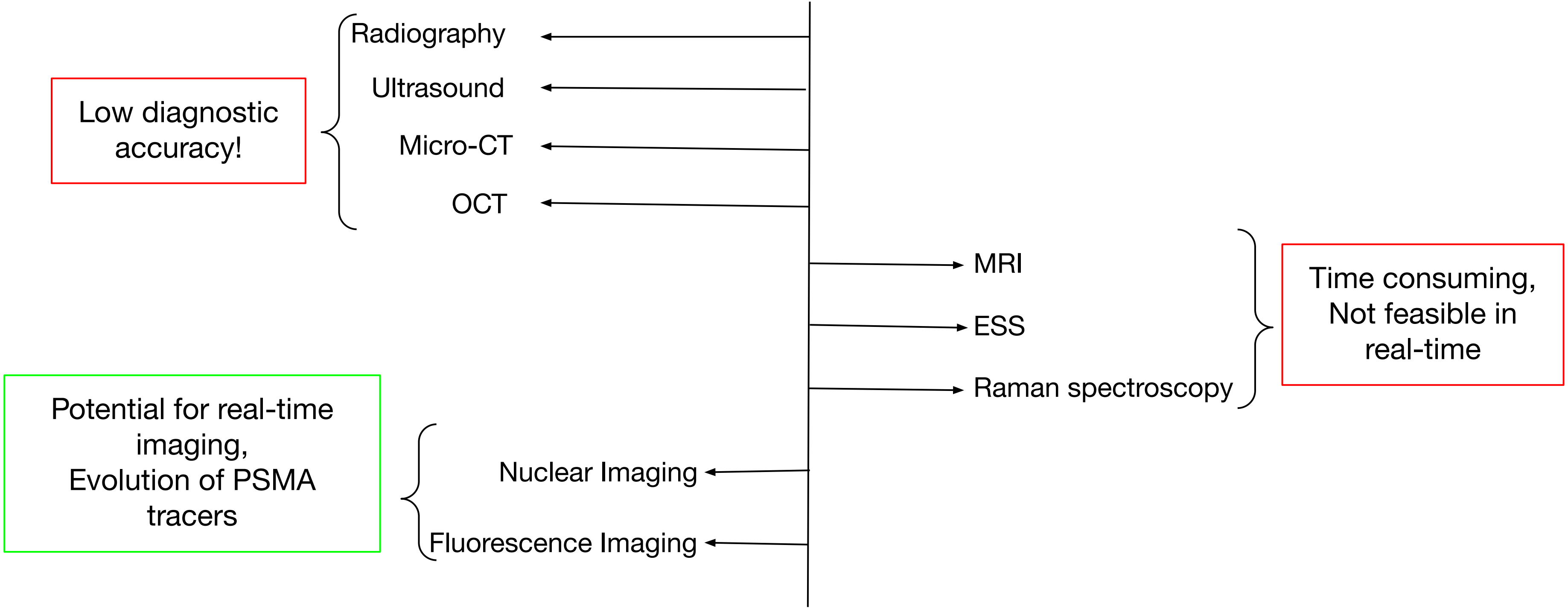

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Relevant research works on resection margin imaging

Low diagnostic accuracy!

- Radiography
- Ultrasound
- Micro-CT
- OCT

Time consuming, Not feasible in real-time

- MRI
- ESS
- Raman spectroscopy

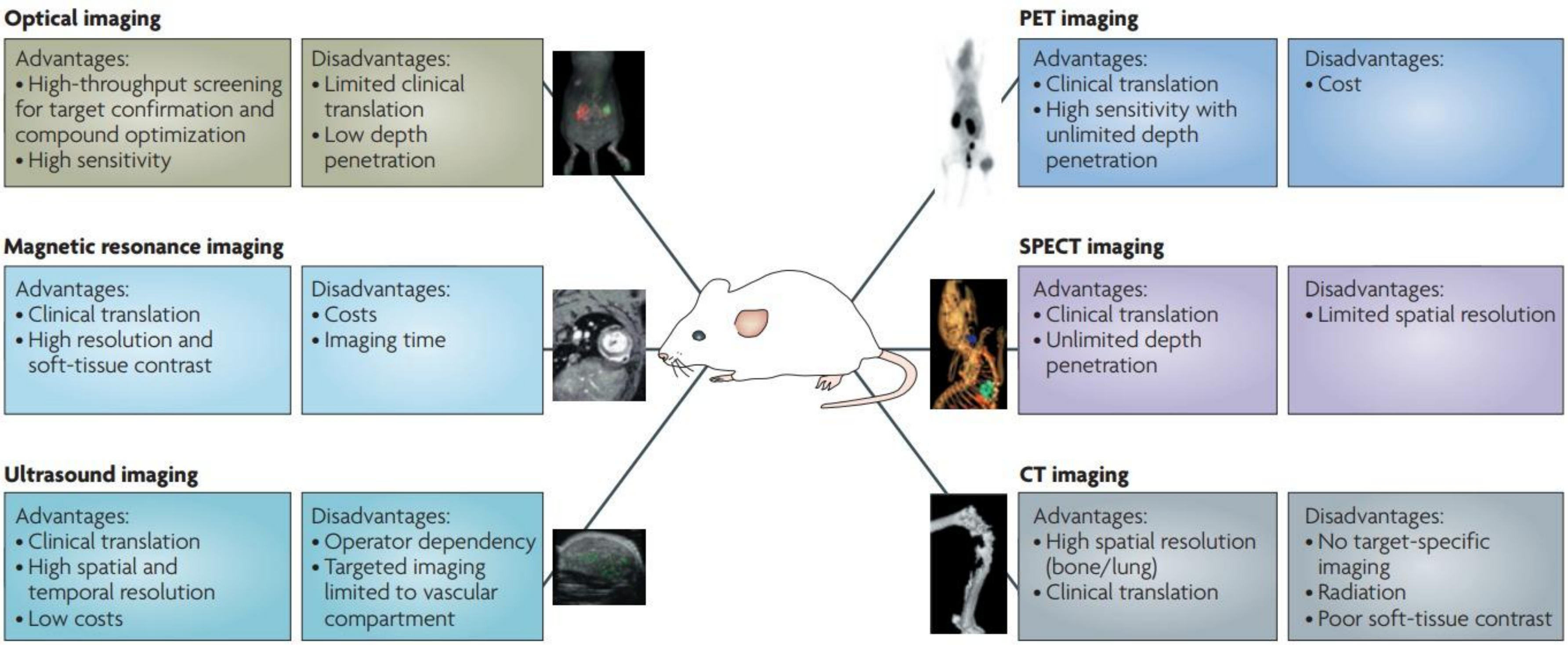
Potential for real-time imaging,
Evolution of FDA tracers

Low spatial resolution (NI);
Low penetration depth (FI)

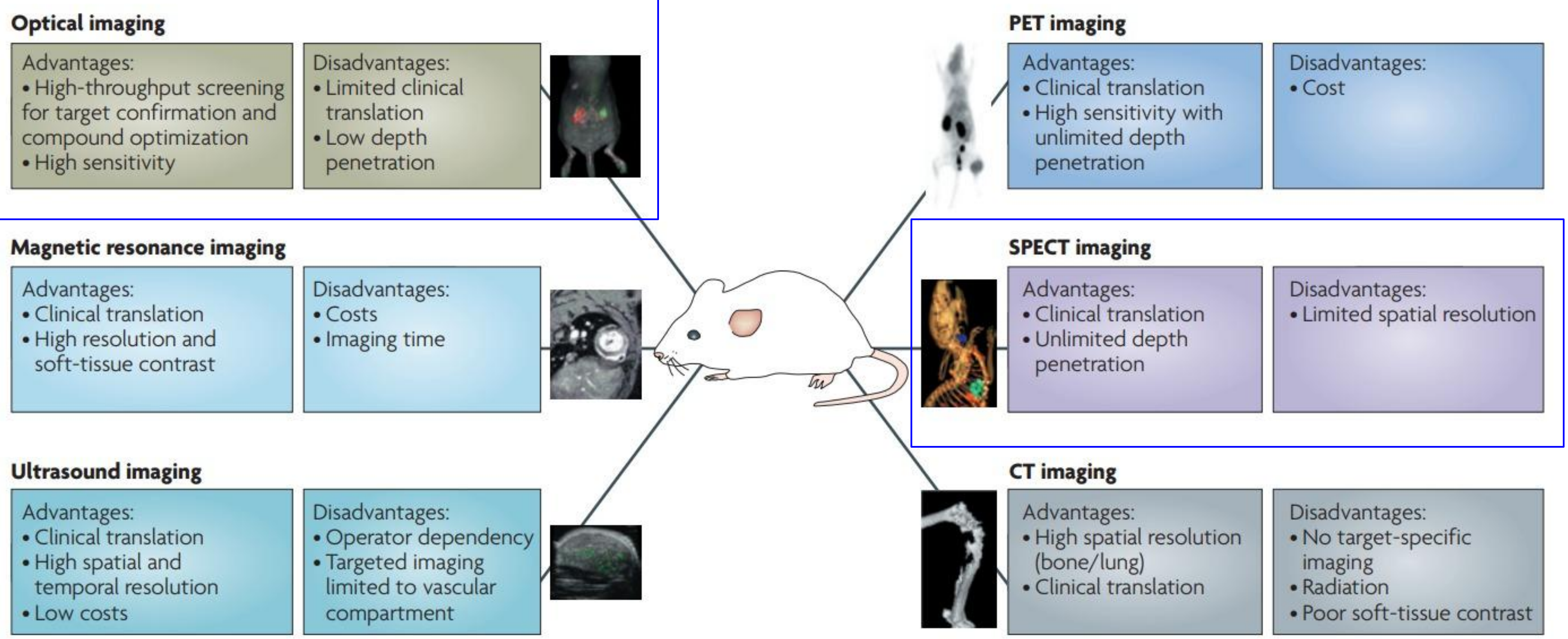
- Nuclear Imaging
- Fluorescence Imaging

[CT: Computed Tomography; OCT: Optical Coherence Tomography; MRI: Magnetic Resonance Imaging; ESS: Elastic Scattering Spectroscopy]

[6] Heidkamp J, Scholte M, Rosman C, Manohar S, Fütterer JJ, Rovers MM. Novel imaging techniques for intraoperative margin assessment in surgical oncology: A systematic review. Int J Cancer. 2021 Aug 1;149(3):635-645. doi: 10.1002/ijc.33570. Epub 2021 May 4. PMID: 33739453; PMCID: PMC8252509.



[7] Willmann JK, van Bruggen N, Dinkelborg LM, Gambhir SS. Molecular imaging in drug development. Nat Rev Drug Discov. 2008 Jul;7(7):591-607. doi: 10.1038/nrd2290. PMID: 18591980.



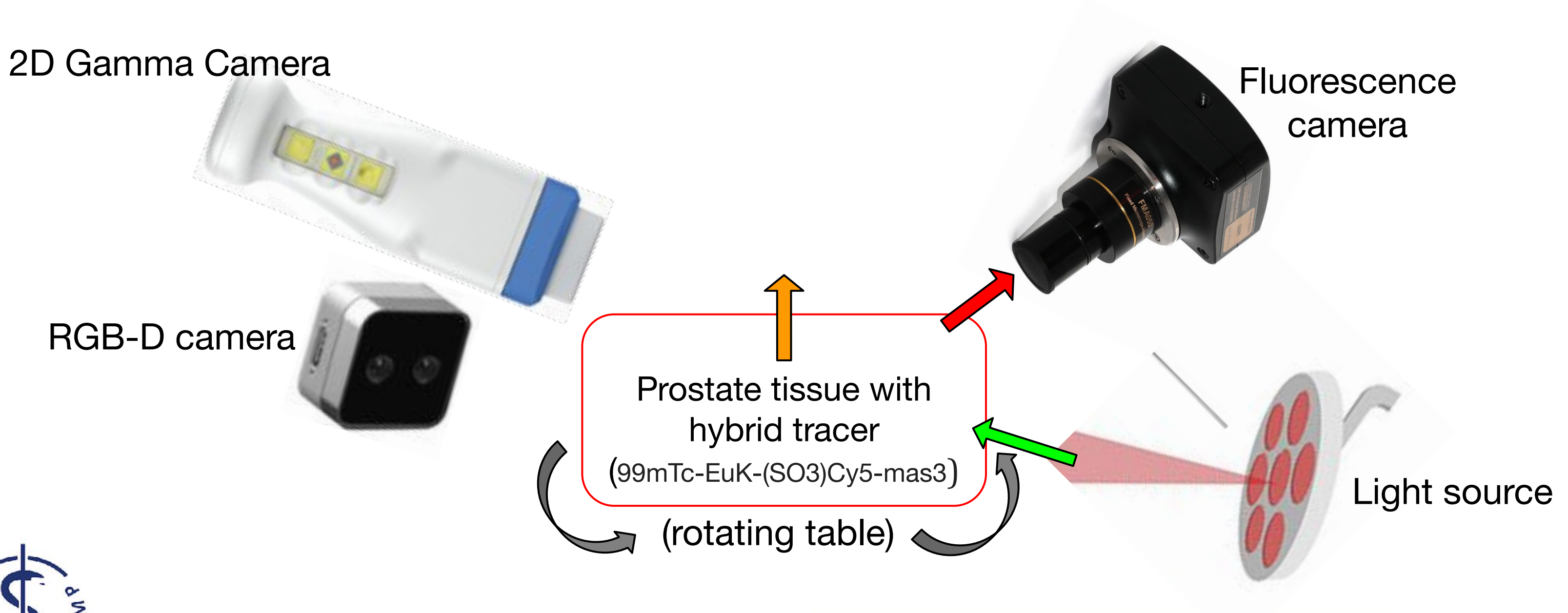
[7] Willmann JK, van Bruggen N, Dinkelborg LM, Gambhir SS. Molecular imaging in drug development. Nat Rev Drug Discov. 2008 Jul;7(7):591-607. doi: 10.1038/nrd2290. PMID: 18591980.

Proposed approach

- Intraoperative analysis of resection margin in real-time at OR (without a pathologist)
- Injecting PSMA (Prostate Specific Membrane Antigen) based tracers into the tissue for precise targeting of prostate cancer cells
- 3D reconstruction volume of the sample using **RGB-D** camera
- **SPECT** for detecting the resection margin of the sample
- **Registration** of SPECT data in the 3D volume
- Accuracy can be enhanced by using a hybrid tracer (SPECT + Fluorescence tracer, Ex: **99mTc-EuK-(SO3)Cy5-mas3**) [8]
- Thus, the proposed solution would be a **hybrid specimen analyzer using SPECT and fluorescence imaging**

[8] Dell'Oglio P, van Willigen DM, van Oosterom MN, Bauwens K, Hensbergen F, Welling MM, van der Stadt H, Bekers E, Pool M, van Leeuwen P, Maurer T, van Leeuwen FWB, Buckle T. Feasibility of fluorescence imaging at microdosing using a hybrid PSMA tracer during robot-assisted radical prostatectomy in a large animal model. EJNMMI Res. 2022 Mar 7;12(1):14. doi: 10.1186/s13550-022-00886-y. PMID: 35254544; PMCID: PMC8901828.

Proposed approach - “system overview”



RGB-D task overview

Depth maps $\rightarrow$ 3D point cloud $\xrightarrow{\text{ICP}}$ 3D model of the prostate tissue

Open3D

SPECT task overview

Step 1: Data (Gamma ray) acquisition using CrystalCam

[Source/Courtesy: Crystal Photonics GmbH]

Step 2: Formation of linear set of equations

$$\boxed{y = Ax}$$

Where, y = Physical measurements

A = System matrix (Each row corresponds to one measurement in our system; Each column represents the different contributions of a particular voxel to the results on each measurement)

x = Quantity we want to reconstruct

SPECT task overview

Step 3: Solving the linear system of equations using MLEM (Maximum Likelihood Expectation Maximization)

$$x_i^{k+1} = x_i^k \cdot \frac{1}{\sum_{j=0}^{J} a_{ij}} \cdot \sum_{j=0}^{J} \frac{y_j \cdot a_{ij}}{q_j}$$

]

$$q_j = \sum_{i=0}^{I} x_i^k \cdot a_{ij}$$

[9] Y. Vardi, L. A. Shepp, and L. Kaufman, "A statistical model for positron emission tomography," Journal of the American Statistical Association, vol. 80, no. 389, pp. 8– 20, 1985

SPECT task overview

Step 3: Solving the linear system of equations using MLEM (Maximum Likelihood Expectation Maximization)

$$x_i^{k+1} = x_i^k \cdot \frac{1}{\sum_{j=0}^{J} a_{ij}} \cdot \sum_{j=0}^{J} \frac{y_j \cdot a_{ij}}{q_j}$$

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Values from the previous iteration (k)

[9] Y. Vardi, L. A. Shepp, and L. Kaufman, “A statistical model for positron emission tomography,” Journal of the American Statistical Association, vol. 80, no. 389, pp. 8– 20, 1985

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Values from the previous iteration (*k*)

coverage factor of the voxel, i.e. how well the measurements included that particular voxel.

[9] Y. Vardi, L. A. Shepp, and L. Kaufman, "A statistical model for positron emission tomography," Journal of the American Statistical Association, vol. 80, no. 389, pp. 8– 20, 1985

SPECT task overview

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Backward projection, and it is the correction factor applied to the voxel

[9] Y. Vardi, L. A. Shepp, and L. Kaufman, “A statistical model for positron emission tomography,” Journal of the American Statistical Association, vol. 80, no. 389, pp. 8– 20, 1985

Timeline & Conclusion 1.1

Literature Research

Components acquisition

Phantom creation

Prototype assembly

RGB-D reconstruction

SPECT reconstruction

Registration of SPECT with RGB-D

Prototype demo

Testing / Validation

System adaptation according to the test results

Finalization

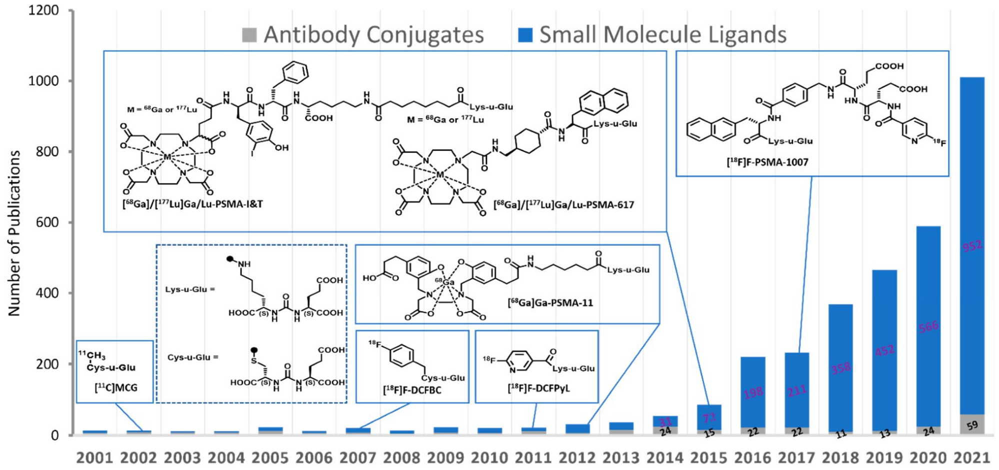
Thesis writing and submission

[TIMELINE SUMMARY (March 2023 - February 2024)]

Initial results / Conclusion 1.2

- Need for the system is high and thus the market potential.
- Research community is very active in this intra-operative field. [6]
- Recent introduction of PSMA based tracers would help us in precise targeting of prostate cells [10]

Trend of Publications of PSMA-targeting Small Molecule Ligands and Antibody Conjugates over 20 Years



(Publications on PSMA-targeting tracers since 2002)

[6] Heidkamp J, Scholte M, Rosman C, Manohar S, Fütterer JJ, Rovers MM. Novel imaging techniques for intraoperative margin assessment in surgical oncology: A systematic review. Int J Cancer. 2021 Aug 1;149(3):635-645. doi: 10.1002/ijc.33570. Epub 2021 May 4. PMID: 33739453; PMCID: PMC8252509.

[10] Abghari-Gerst M, Armstrong WR, Nguyen K, Calais J, Czernin J, Lin D, Jariwala N, Rodnick M, Hope TA, Hearn J, Montgomery JS, Alva A, Reichert ZR, Spratt DE, Johnson TD, Scott PJH, Piert M. A Comprehensive Assessment of 68Ga-PSMA-11 PET in Biochemically Recurrent Prostate Cancer: Results from a Prospective Multicenter Study on 2,005 Patients. J Nucl Med. 2022 Apr;63(4):567-572. doi: 10.2967/jnumed.121.262412. Epub 2021 Jul 29. PMID: 34326126; PMCID: PMC8973291.


Thank you for your attention!
Any questions?