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Radiopharmaceuticals, AI and predictive analytics: Revealing hidden insights

13 March 2024

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Agenda

01 Telix and Radiopharmaceuticals

02 AI in healthcare and medical imaging

03 Role of AI at Telix

04 Clinical Decision Support – AI Platform for Predictive Analytics

05 Questions and Discussion

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Telix: A global leader in radiopharmaceuticals

Theranostics for oncology and rare diseases

COMMERCIAL STAGE IMAGING PORTFOLIO

- Illuccix® for prostate cancer imaging launched in U.S. & AU/NZ
- Preparing regulatory filings for two additional products

INDUSTRY LEADING THERANOSTIC PIPELINE

- Late-stage imaging and therapeutic assets
- Supported by extensive clinical data
- >20 active clinical studies across eight indications

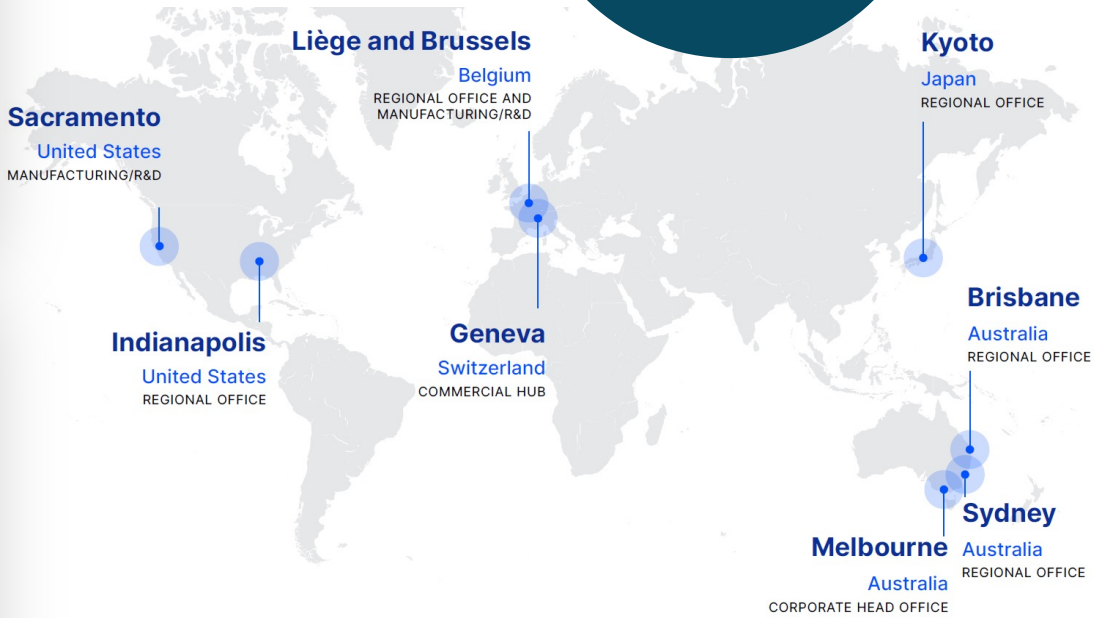
ADVANCED SUPPLY CHAIN & MANUFACTURING

- World-leading distribution and supply partners
- Delivering patient-doses globally
- Manufacturing facility in EU
- In-house radiochemistry development and clinical dose production (Optimal Tracers)

A GLOBAL BUSINESS

- ~380 employees globally
- Headquartered in Melbourne, Australia
- Regional offices in U.S., Switzerland, Belgium and Japan
- Commercial revenue funding R&D

Global nuclear medicine market growth forecast: US$6B in 2021 to $35B by 2035



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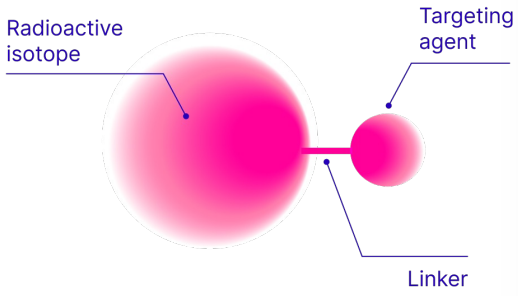
The theranostic approach

Using imaging and therapy to deliver personalised, precision medicine

01

Targeted radiation drug



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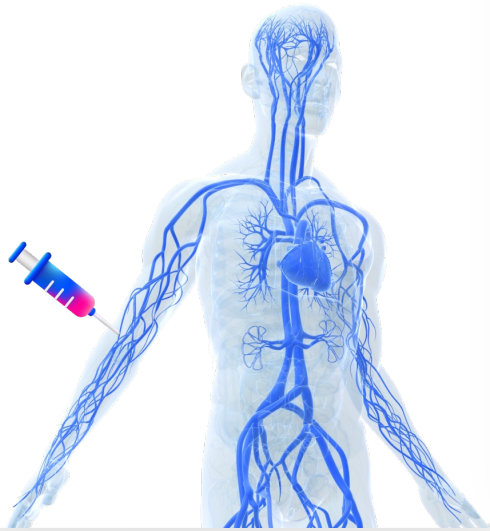
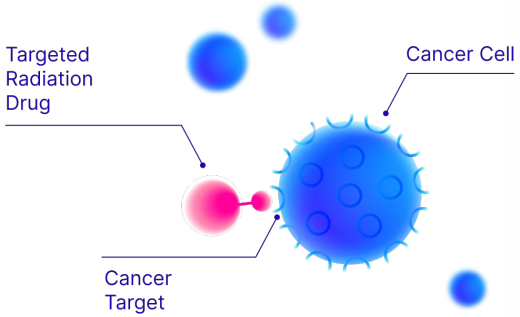
Intravenous injection



03

Targeted delivery



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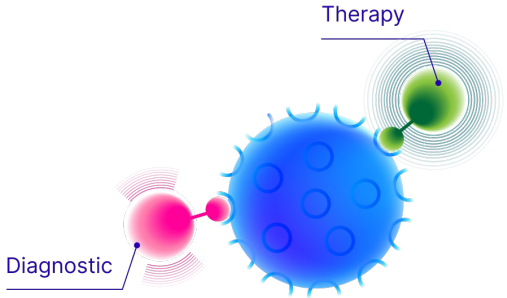
See it. Treat it.



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Core pipeline: Oncology and rare diseases

	TARGETING AGENT	ISOTOPE	Dx/ Tx	PHASE 1	PHASE 2	PHASE 3	COMMERCIAL	UPCOMING MILESTONES
Prostate PSMA[1]	Antibody	^{177}Lu	Tx	TLX591 (^{177}Lu rosopatamab tetraxetan)				ProstACT GLOBAL interim readout: Q1 2025
	Antibody	α (alpha)	Tx	TLX592 (alpha-RADmAb®)				Phase 1 CUPID trial results: H1 2024
	Small molecule	^{68}Ga	Dx	TLX591-CDx (^{68}Ga-PSMA-11, Illuccix®)				EU approval decision: H1 2024 Phase 3 China bridging study complete: H2 2024
Kidney CAIX[2]	Antibody	^{177}Lu	Tx	TLX250 (^{177}Lu-girentuximab)				Phase 2 trial data readouts: H2 2024
	Antibody	^{89}Zr	Dx	TLX250-CDx (^{89}Zr-girentuximab, Zircaix™*)				FDA approval decision: H2 2024
Brain LAT-1[3]	Small molecule	^{131}I	Tx	TLX101 (^{131}I-IPA)				Phase 1 IPAX-2 trial data readout: H1 2025
	Small molecule	^{18}F	Dx	TLX101-CDx (^{18}F-floretyrosine, Pixclara™*)				FDA approval decision: H2 2024
STS[4] PDGFRα[5]	Antibody	Undisclosed	Tx	TLX300 (-olaratumab)				Phase 1 trial commencement: H1 2024
	Antibody	^{89}Zr	Dx	TLX300-CDx (^{89}Zr-olaratumab)				
BMC[6] CD66[7]	Antibody	^{90}Y	Tx	TLX66 (^{90}Y-besilesomab)				Phase 2 trial commencement: H1 2024
	Antibody	^{99m}Tc	Dx	TLX66-CDx (^{99m}Tc-besilesomab, Scintimun®[8])				

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*Note: Nominated brand name subject to final regulatory approval.

1. Prostate-specific membrane antigen.
2. Carbonic anhydrase IX.
3. L-type amino acid transporter 1.
4. Soft tissue sarcoma.
5. Platelet derived growth factor receptor alpha.
6. Bone marrow conditioning.
7. Cluster of differentiation 66.
8. Marketed under license by Curium Pharma.

The role of AI in healthcare and medical imaging

Despite major advances, challenges remain in routine clinical diagnosis

The increased use of medical imaging is creating multiple workforce challenges:

- **Manual image processing** and clinical “reading” is a **highly specialised and time-consuming** task
- Clinicians do not have time to **extract all relevant information** from images and therefore the **full value of data** is **not being utilised**
- There is potential for **differential interpretation** between clinicians for image-based diagnosis
- **Longitudinal analysis** of images (over time) is critical to monitoring disease progression and treatment response

AI can help to overcome these challenges and optimise image-based diagnosis:

- Enables clinicians and institutions with routine tasks to become **more efficient**, and manage **more patients** in a timely manner
- Helps clinicians **better understand data** presented and **assists with harmonisation and interpretation**, especially identifying even small trends/changes over time
- Enables the clinician to make **more accurate** and standardize **quantitative disease diagnosis**
- Provides **personalised disease predictions** such as risk, optimised treatment options and response

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Role of AI at Telix

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Role of AI at Telix

Earlier, more accurate diagnosis, and personalised disease predictions

Diagnosis, prediction and productivity

A platform that addresses key clinical and workforce needs:

- **Image reading:** Automated lesion segmentation and classification
- **Clinical decision support:** Personalised medicine
- **Clinical trial efficiency:** e.g. patient selection and productivity improvement

Aligned to our theranostic pipeline

- Applicable to multiple disease indications, e.g. prostate, kidney, glioma
- **Further enhances the value of imaging – can interpret complex data** from multiple sources to **inform clinical decisions**
- Extracting **greater utility** out of data from previous and ongoing clinical trials

Commercial edge

- Favourably **differentiated from competitor solutions**
- Ability to **rapidly build** applications
- **Near-term** regulatory submissions are feasible based on the maturity level of the current platform and technology

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Supercharging our AI platform

Our platform adds a new dimension of clinical support

Reader Support

Increases efficiency and reproducibility of imaging assessments:

- Automates lesion segmentation and differentiates physiological uptake
- Potential to identify lesions of low PSMA SUV (<3) uptake
- Future potential to track individual lesions between scans to show changes over time

Clinical Decision Support

Predicts disease outcomes including potential risk, severity and response to treatment:

- Automated machine learning (AutoML) platform can generate indication-specific applications for use with PET and other imaging modalities
- Predictive capabilities differentiated from commercially available AI solutions
- In prostate cancer can reliably predict a patient's "Gleason score" from an Illuccix® PET scan
- Potential to apply the model to new indications

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Clinical Decision Support – AI Platform for Predictive Analytics

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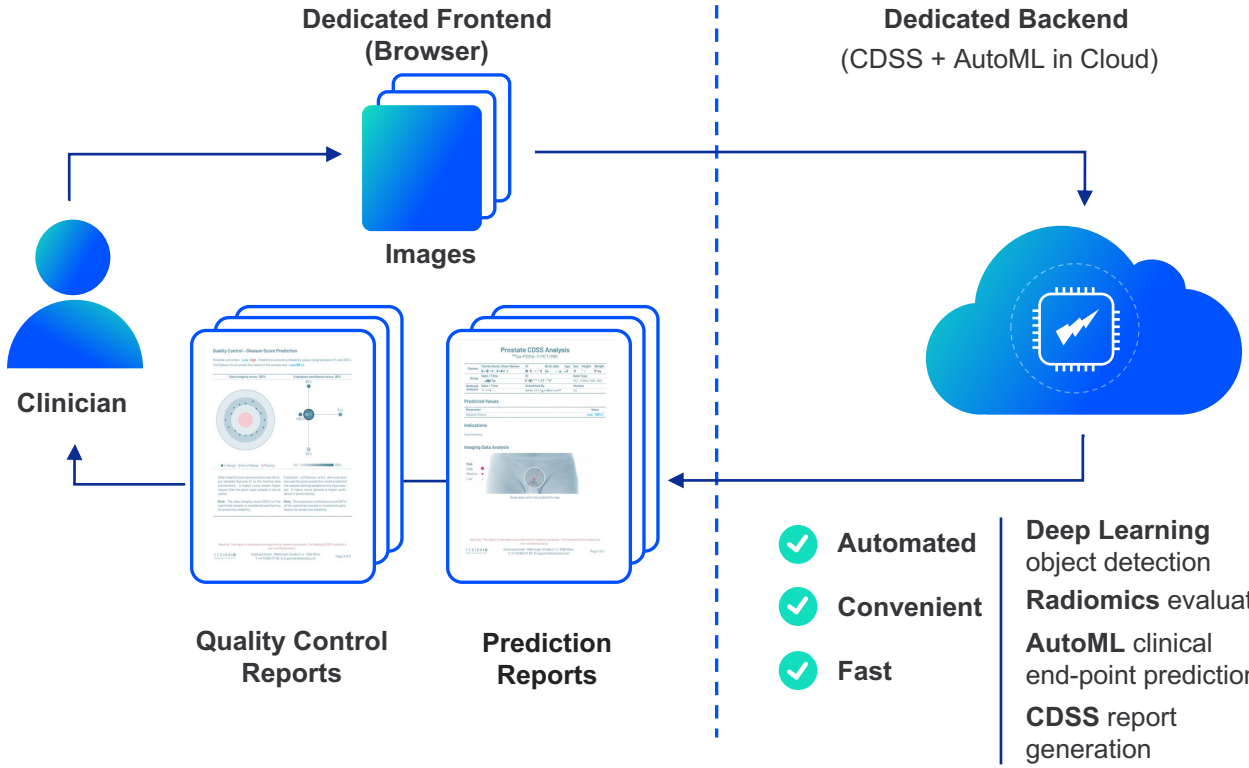
Clinical decision support designed for nuclear medicine

Enhances predictive capabilities of Telix's AI platform

Two major components of the platform

- **Clinical Decision Support System (CDSS):** Rapidly generates indication-specific applications from available datasets
- **Automated Machine Learning (AutoML):** "Zero code" approach greatly reduces time, cost and level of expertise required to build, test and validate AI models from raw data

- Unique capability in the market and provides advanced AI modelling opportunities
- Proof of concept developed for prostate, breast and lung cancer[1]
- **First application – predicting Gleason score for primary prostate cancer**, with potential to develop multiple applications across a variety of disease areas



1. Papp, L et al. Journal of Nucl Med. 2018; Papp, L et al. European Journal of Nucl Med and Mol Imaging. 2021; Zhao, M et al. European Radiology. 2022; Krajnc, D et al. Cancers. 2021; Papp, L, Journal of Nucl Med. 2019.

Prostate Cancer

Clinical Standard of Care and Management

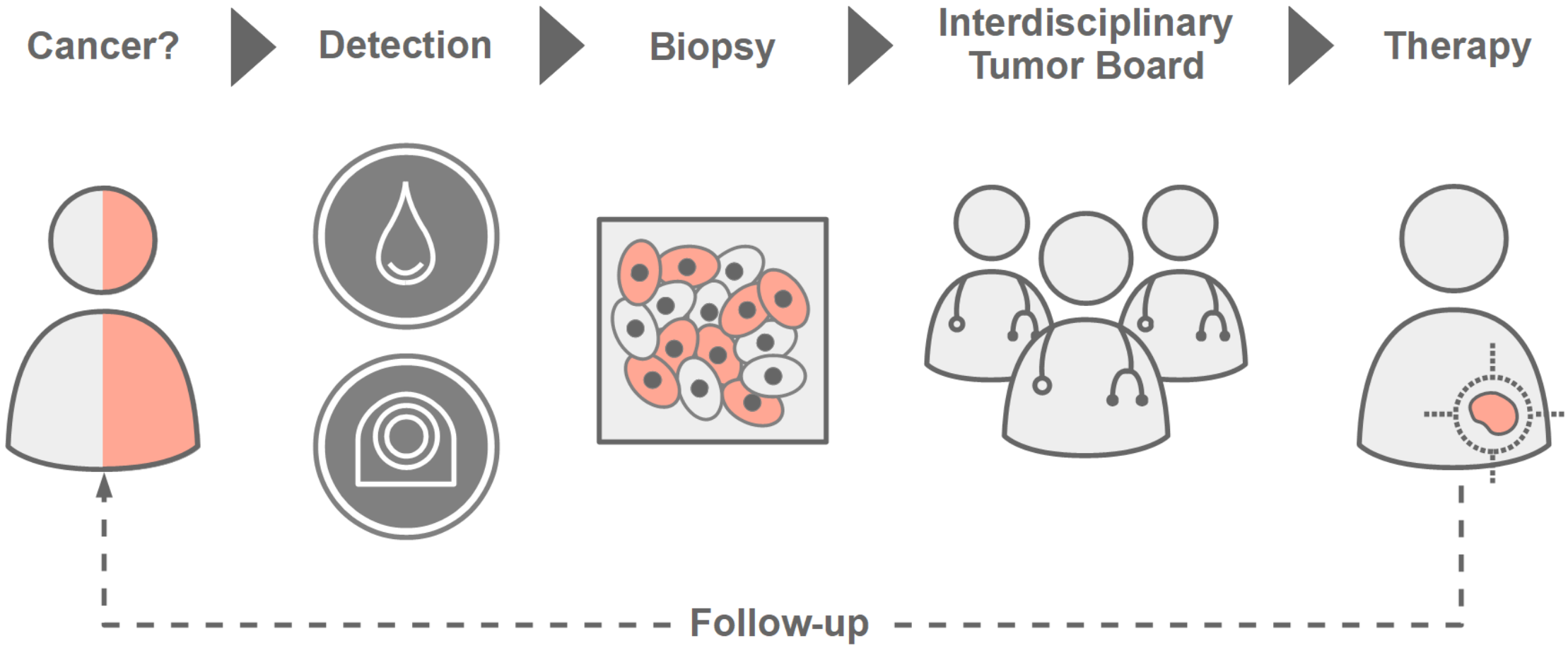


Image courtesy L. Papp

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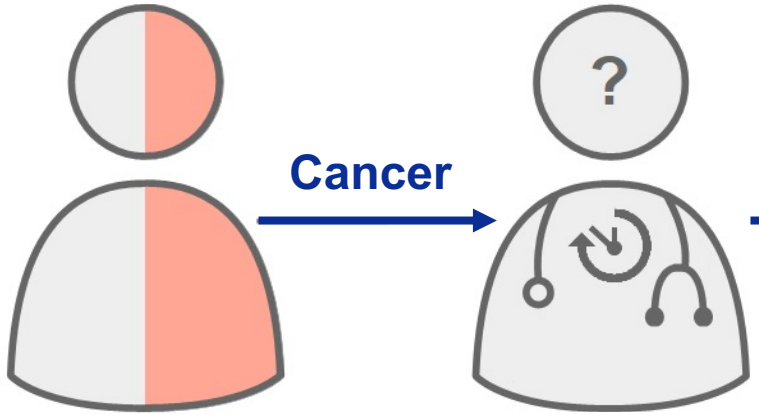
Prostate Cancer

Long term challenges



Cancer → High-risk? → Radical prostatectomy → 5-10 years → Recurrence

Many patients go through unnecessary removal

Major effect on quality of life

20-40% chance even if prostate was removed

Image courtesy L. Papp

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Prostate Cancer

Biopsy required to confirm diagnosis and risk assessment

Tumours are heterogeneous:

- → Each biopsy cell sample is examined and assigned differentiation degree – Gleason Pattern (1-5)
- → Two most common Gleason Patterns are summed to provide the Gleason Score (e.g. 3+4, 4+3)
- → Biopsy takes only small samples and analysis can be subjective
- → **Inaccurate diagnosis** (~60% accurate)[1]

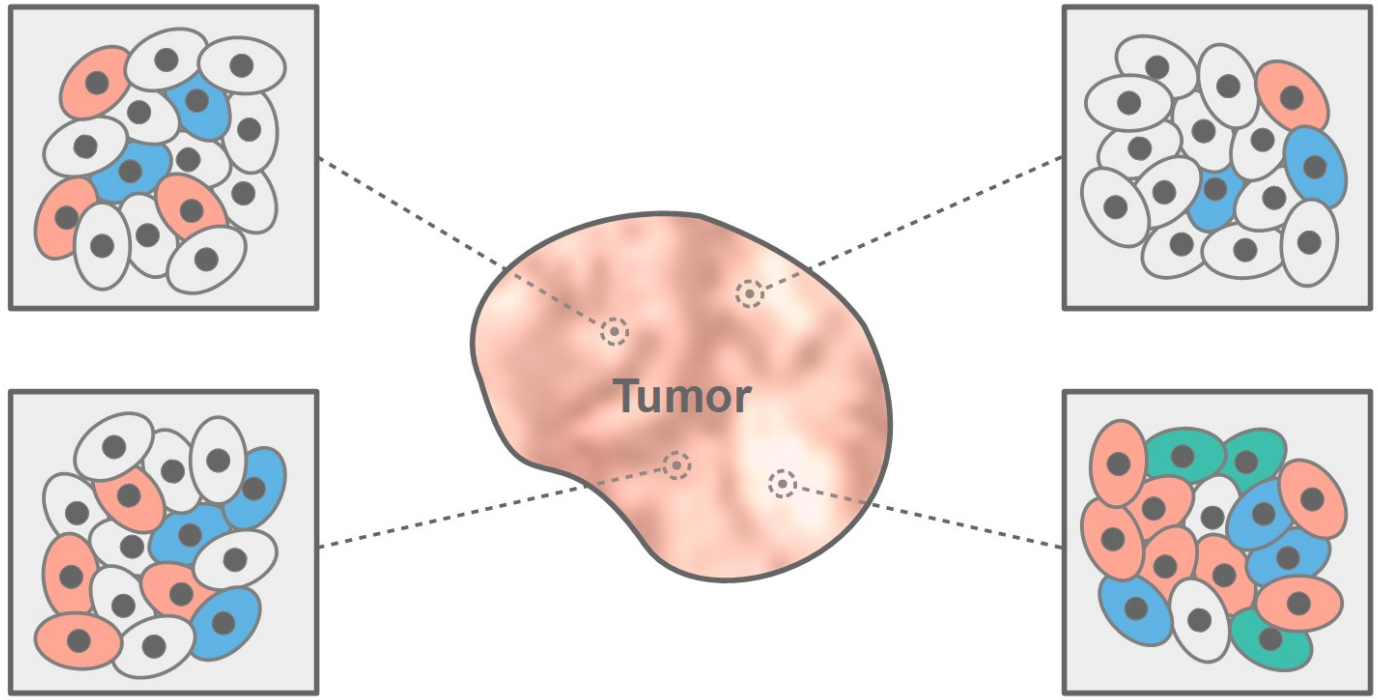


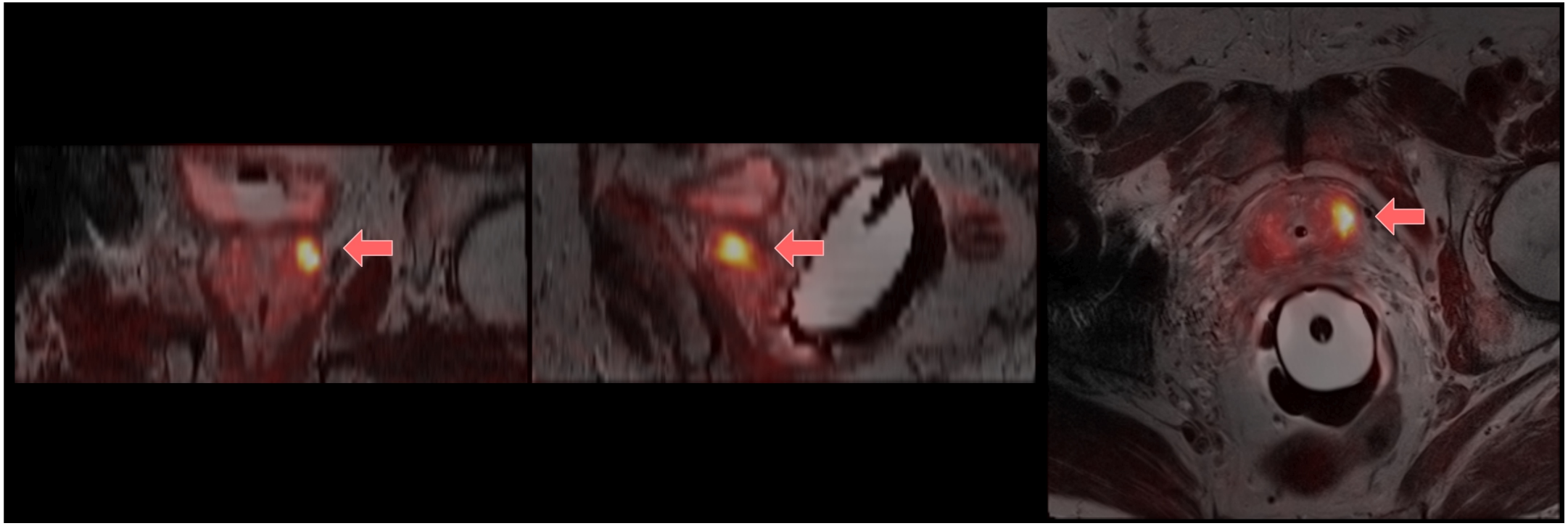
Image courtesy L. Papp

1. Papp L, et al. Personalizing Medicine Through Hybrid Imaging and Medical Big Data Analysis. Front Phys [Internet]. 2018 Jun 7;6.

Prostate Cancer

Hybrid Imaging – structural and functional

Shows tumour heterogeneity, but with a lower resolution compared to biopsy



Primary prostate ^{68}Ga-PSMA-11 (Illuccix®) PET/T2w MRI case fused and visualized with oblique coronal, sagittal and axial views.

Image courtesy L. Papp

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Radiomics

The process to extract a high-throughput of **numerical features** from medical images for **characterising diseases** *in vivo*

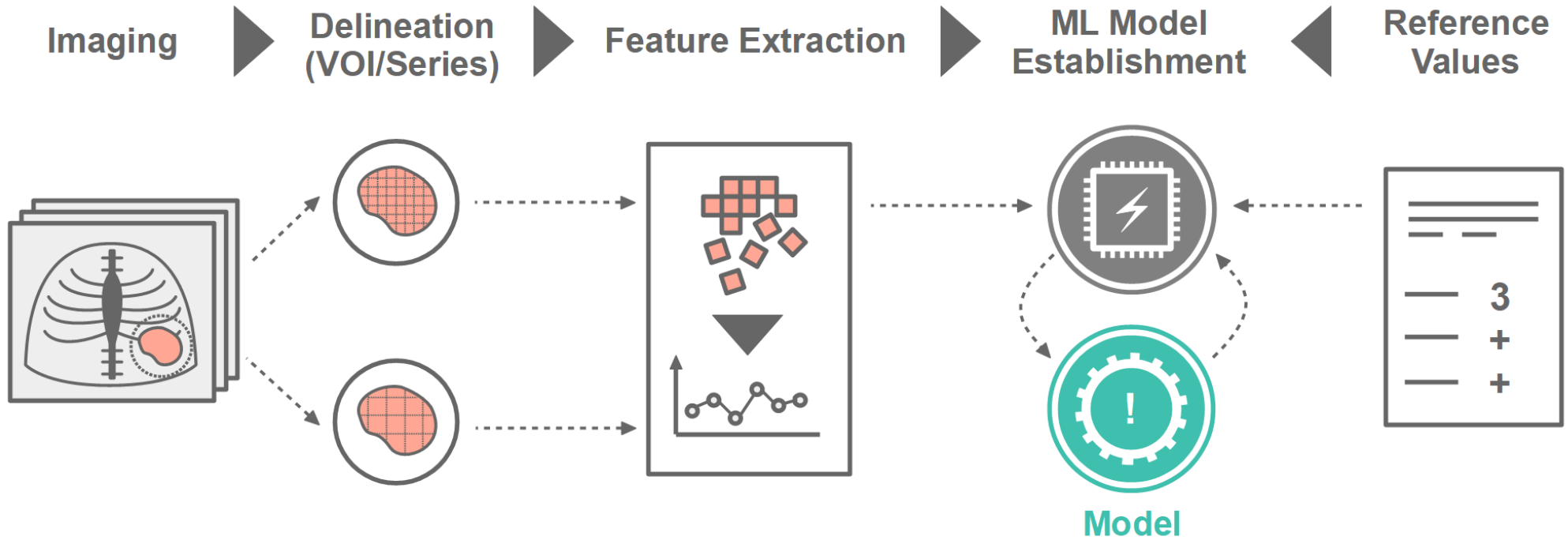
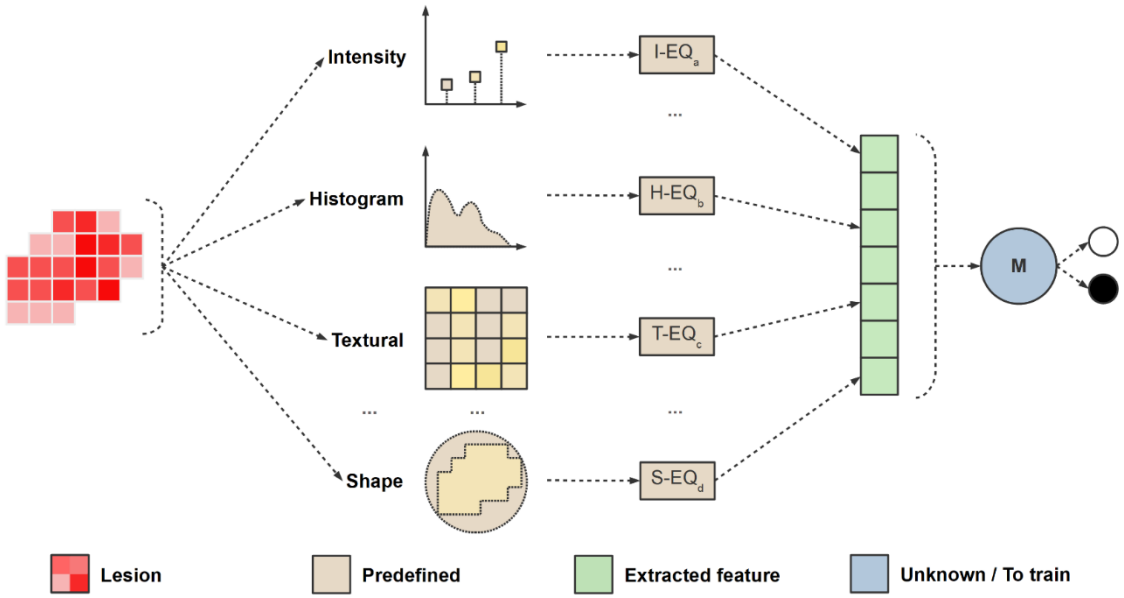


Image courtesy L. Papp

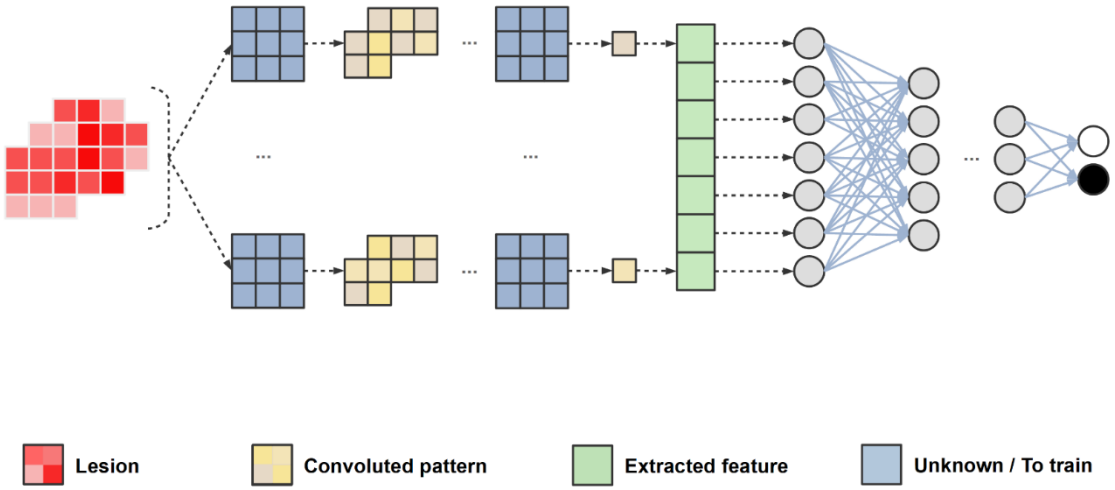
Shallow vs. Deep Radiomics

Shallow Radiomics (Radiomics + ML)



- **Handcrafted** features
- Analysis by traditional machine learning (ML)
- **Simple**, shallow models (10 – 100+ parameters)
- **Moderate-high** predictive performance

Deep Radiomics (Convolutional Neural Networks)



- **Learnt** features
- Analysis by **convolutional** + **neural network** layers
- **Complex** models (100k - 1M+ parameters)
- **High** predictive performance

Images courtesy L. Papp

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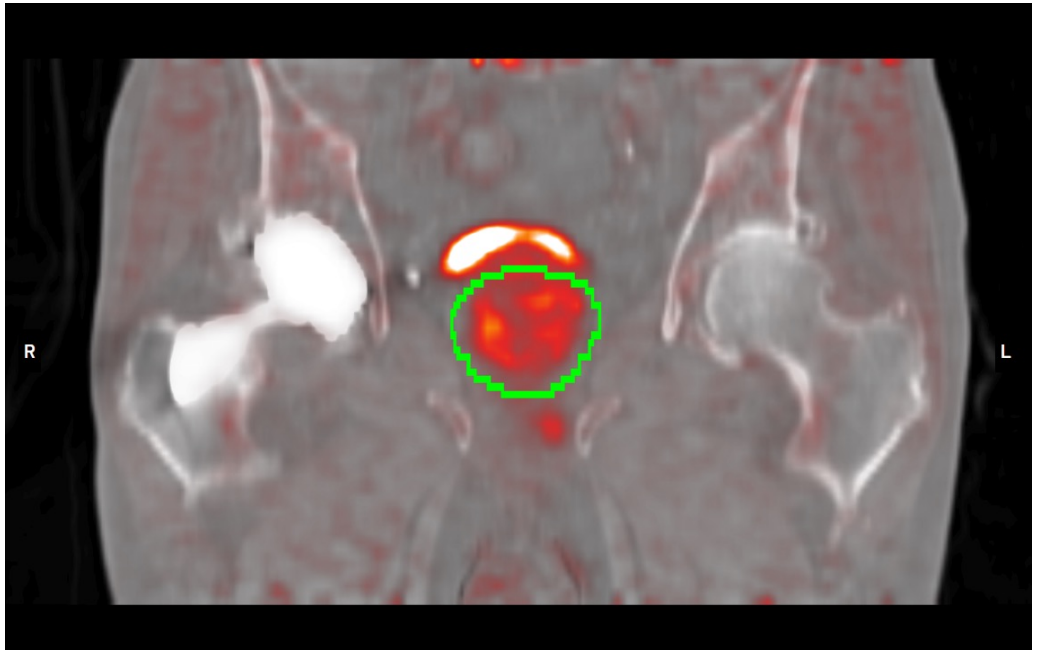
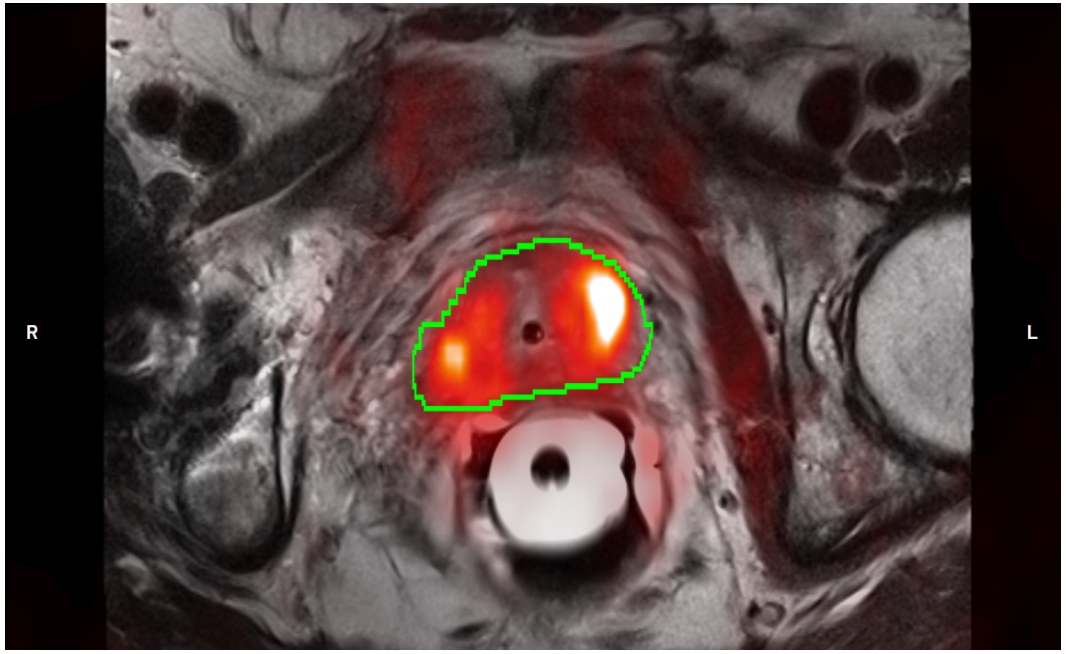
Prostate Organ Detection with Deep Learning (DL)



^{68}Ga-PSMA-11 (Illuccix®) PET/CT fused coronal view with detected prostate overlaid (green border)



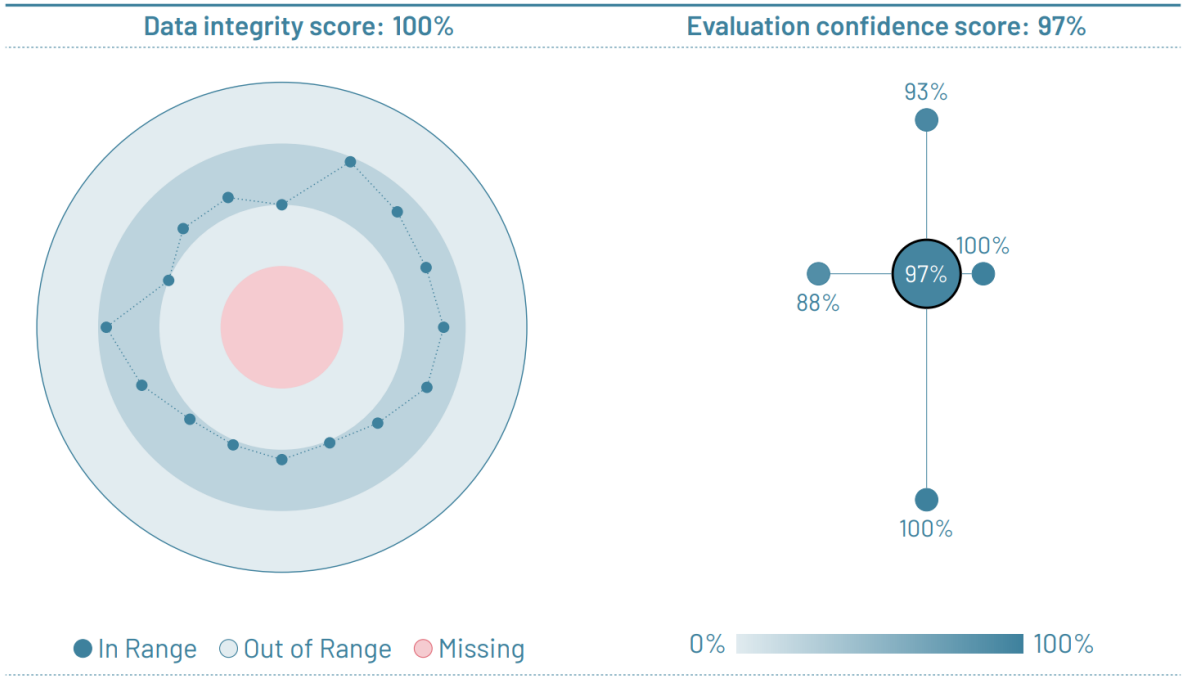
^{68}Ga-PSMA-11 (Illuccix®) PET/MRI fused oblique-axial view with detected prostate overlaid (green border)

Actual images from the Primary Prostate Cancer CDSS application of Telix Pharmaceuticals

Characterisation of Lesions with Radiomics

CDSS Outputs – Prediction and confidence in clinical decision making

^{68}Ga-PSMA-11 (Illuccix®) PET/CT cinematic volume rendering (CVR) view with detected prostate, lesion probability map and Gleason Score prediction



Quality control report (part) representing data integrity and evaluation confidence certainties made for prediction

Actual images from the Primary Prostate Cancer CDSS application of Telix Pharmaceuticals

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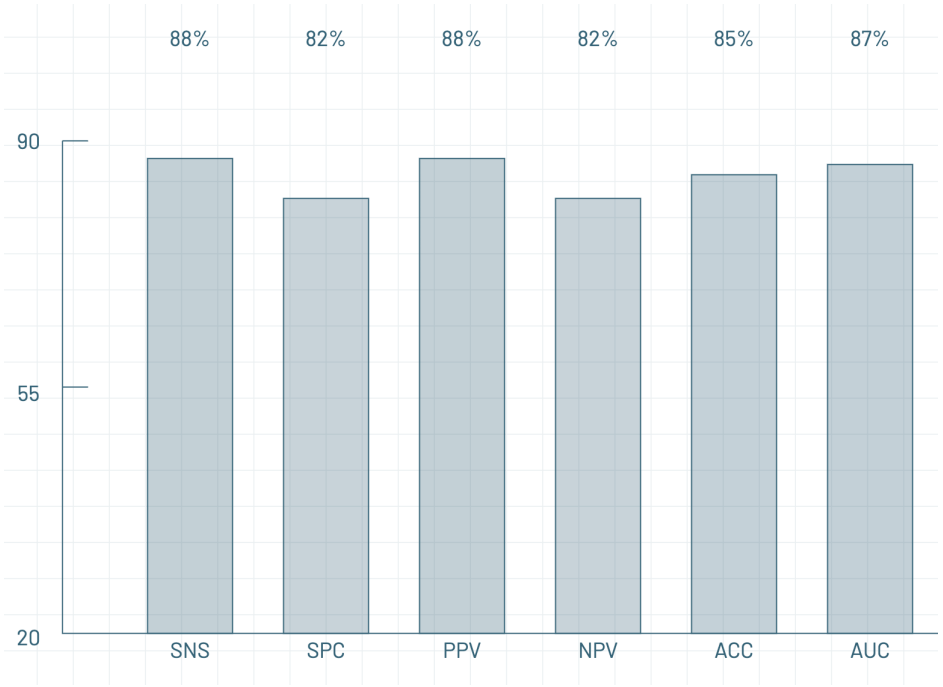
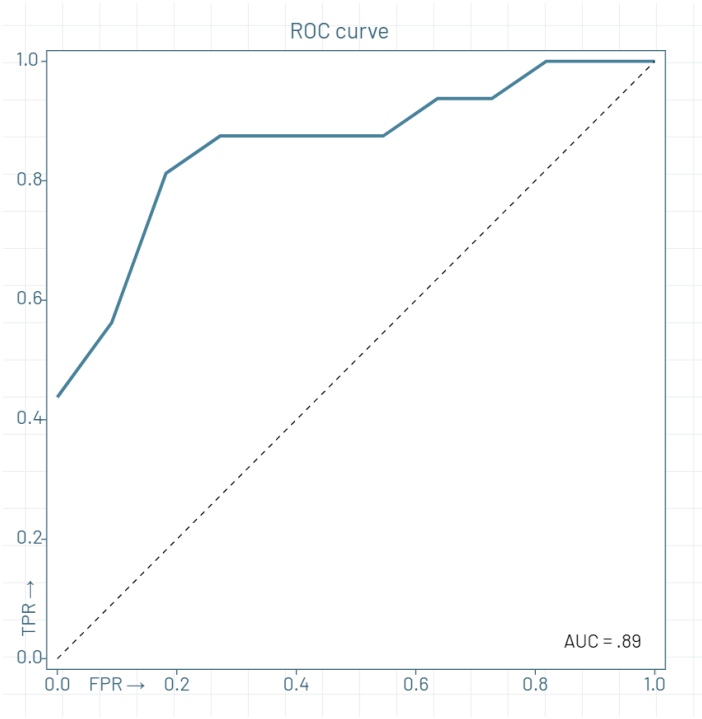
Gleason Prediction Results – Primary Prostate Cancer CDSS

AutoML performance outputs

Training: 50 PET/CT with **31** Radiomic Features extracted
Test: 24 PET/MR
Balanced dataset: 50% Gleason ≤ 7
50% Gleason > 7

High-ranking features (name)	Mean Ranking
PSMA-TBR.01.ih.entropy	10
PSMA-SUV.01.stat.iqr	8
PSMA-TBR.01.cm.joint.entr	7
PSMA-TBR.01.cm.inv.diff.mom.norm	6
PSMA-TBR.01.ngt.coarseness	6
PSMA-SUV.01.stat.mean	6
PSMA-TBR.01.cm.info.corr.1	6
PSMA-TBR.01.cm.inv.diff.norm	5
PSMA-TBR.01.ih.mean	4
PSMA-SUV.01.stat.max	3
PSMA-TBR.01.stat.iqr	3
PSMA-SUV.01.morph.comp.1	3
PSMA-TBR.01.ngt.busyness	3
PSMA-SUV.01.stat.var	3
PSMA-SUV.01.morph.asphericity	3
PSMA-TBR.01.ngt.complexity	2
PSMA-SUV.01.stat.min	2
PSMA-TBR.01.ngt.strength	2
PSMA-TBR.01.cm.clust.shade	2
Rest of features	16





Actual images from the AutoML application of Telix Pharmaceuticals

SNS – Sensitivity; SPC – Specificity; PPV – Positive Predictive Value; NPV – Negative Predictive Value; ACC – Accuracy; AUC – Area Under the Receiver Operator Characteristics Curve; TPR – True Positive Rate; FPR – False Positive Rate

Primary Prostate Cancer CDSS

Outcomes and Conclusion

- Biopsy is the clinical standard of diagnosing prostate cancer
- Hybrid imaging, particularly ^{68}Ga-PSMA-11 (Illuccix®) PET with CT or MRI can characterize tumour heterogeneity in vivo
- It is feasible to detect the primary prostate from CT or MRI and suspicious lesions in ^{68}Ga-PSMA-11 (Illuccix®) PET with deep learning
- It is feasible to predict Gleason Score 3+4 (low) vs 4+3 (high) cases built on radiomics and AutoML
- Such cloud AI solutions could have a significant impact in prostate cancer management in the near-future

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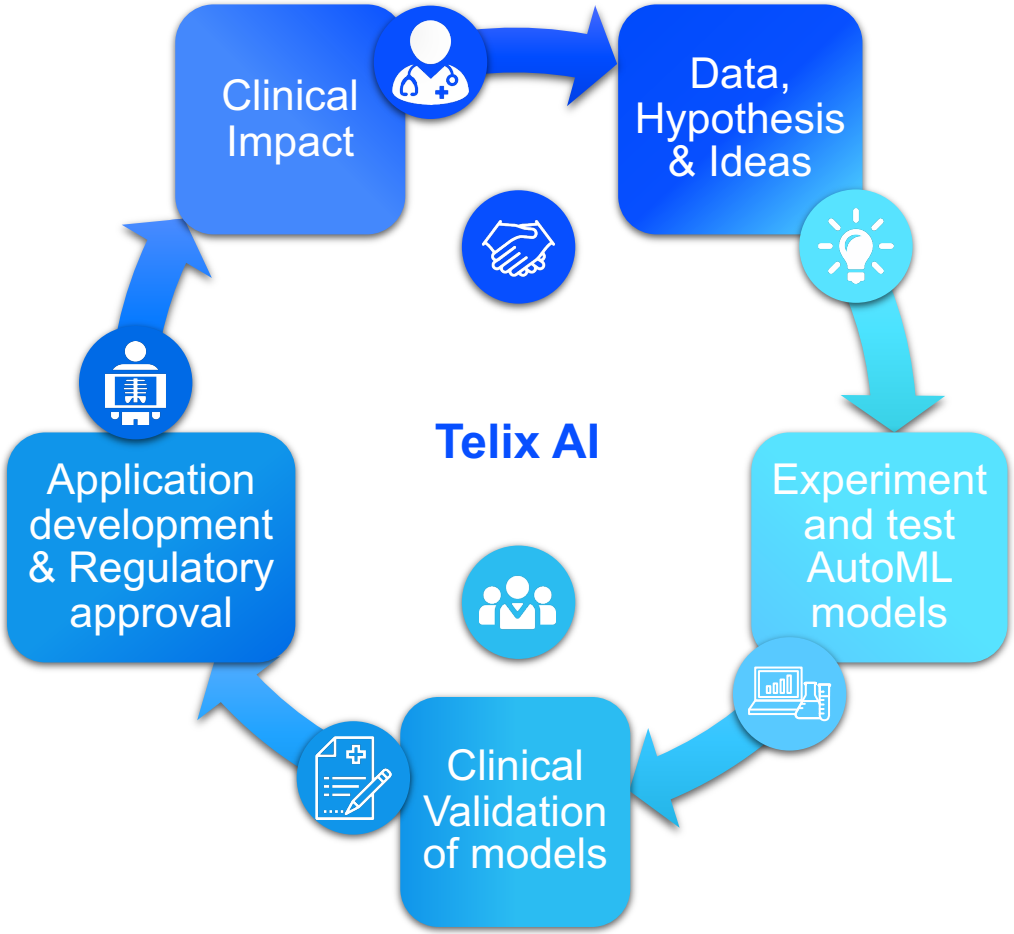
Benefits of CDSS to Telix and Clinical/Research Community

Research tool to validated clinical decision support

- Data – diagnostic imaging, clinical information, outcomes, etc.
- Hypothesis (IITs) – treatment response, disease grading, progression, etc.
- Collaboration to build, test and validate AutoML/CDSS predictive models
- Release new CDSS application with imaging or therapy launch

- **Example – Glioblastoma (GBM) Risk status (collaboration with European academic institution):**
  - FET-PET images, with ground-truth histology results
  - Build segmentation model ⟶ extract radiomics ⟶ train AutoML model ⟶ predict risk status ⟶ validate with histology data



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A powerful AI development platform

Greatly enhances Telix's ability to rapidly generate new applications from imaging data

Favourably differentiated from competitor solutions	• Current AI solutions in nuclear medicine can support interpretation and reading of images – but lack prediction capability
Clinically focused	• Secure, transparent, and trusted; quality control reports accompanying each output provide a data integrity and evaluation confidence score
Strong alignment with Illuccix® and Telix theranostic pipeline	• Driven by diagnostic imaging for predictive and prognostic capabilities, beyond just Illuccix®
Speed to market for new CDSS applications	• No computer coding expertise required to go from clinical hypothesis, to experimentation, validation and product

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Clinical Decision Support: Next steps

Go-to-market strategy

Regulatory filing

- Near-term availability to key opinion leaders as a research tool, establish validation data sets for key applications
- Regulatory submissions (FDA 510(k) and MDR CE Mark) for platform and primary prostate cancer CDSS application planned

Clinical alignment

- Build CDSS application supported by Illuccix® for advanced prostate cancer with appropriate data
- Upon approval launch CDSS application into the appropriate markets
- Integrate existing and new algorithms into software platform

Indication expansion

- Build CDSS applications for other agents relevant to Telix's pipeline
- Develop predictive algorithms that link imaging to therapeutic outcomes by harnessing data

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Questions & Discussion

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