Software Assessment for Radiotheranostics Applications: Key Features, Challenges, and Future Prospect

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Disclosures

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Introduction

- Regulatory **health technology assessment (HTA)** frameworks evaluate the **safety of radiotheranostics** (**handling and administration)**.
- HTA prioritizes **safety over clinical outcomes,** overlooking the potential of patient-tailored treatments, **neglecting optimal efficacy.**
- **Software in radiotheranostics** facilitates **personalized treatment planning** and ensures **the safety of individual patients.**

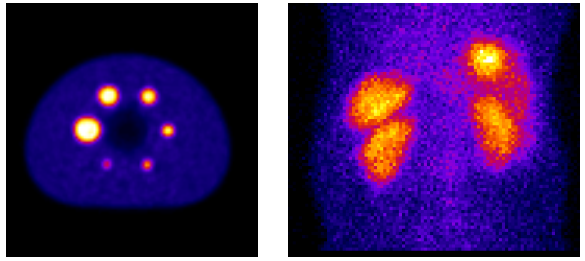


Image quantification

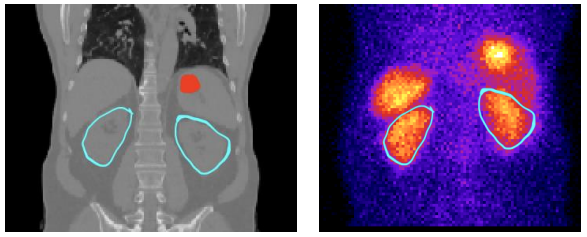
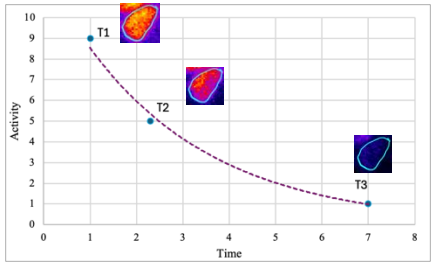


Image segmentation & registration



Dose calculation

Introduction

- Several software solutions embed **AI-based methods** for segmentation, registration, and/or single time-point dose estimation.
- **AI-based health technologies** challenge the applicability of traditional HTA methods.
  - AI-based models usually evolve (or not)
  - Lack of transparency (explainability, interpretability)
  - Difficulty in testing/replicability (need for benchmark datasets)
  - Lack of traceability & auditability (logs, version)
  - Ethical and legal implications

DI BIDINO et al. (2024). Int. J. Technol. Assess. Health Care

Aims

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- How can we apply the **HTA framework to radiotheranostics software** solutions?
- How can we assess a radiotheranostics software solution for radiotheranostics in a **clinical environment**?

HTA framework

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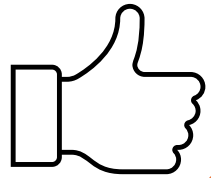
- Definition of Scope and Context
- Technical and Analytical Performance
- Clinical Effectiveness
- Safety
- Economic Evaluation
- Organizational Impact
- Legal, Ethical, and Social Implications
- Evidence Appraisal and Uncertainty
- Recommendations and Decision-Making

WHO HTA of Medical Devices (2023)

HTA framework

Definition of Scope and Context

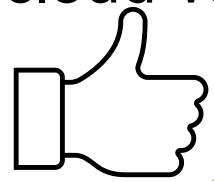
- **Technology description**: Identify the software solution, version, dose calculation, imaging modalities, inputs, # time-points, and tools.
- **Comparator(s)**: Similar segmentation software; similar dosimetry software.
- **Clinical indication**: Types of radionuclide therapy (^{177}Lu-PSMA, ^{131}I, ^{90}Y microspheres).
- **Stakeholders**: Medical physicists, nuclear medicine physicians, patients, IT administrators, and regulators.
- **Perspective**: Public hospital, private health system.



HTA framework

Technical and Analytical Performance

- **Validation studies**:
  - Accuracy of absorbed dose calculations vs. reference phantoms or MC simulations (RAMONAHENG et al. 2022; GRASSI et al. 2024; MORPHIS et al. 2025).
  - Precision and reproducibility across users and datasets (SNMMI Lu-177 Dosimetry Challenge 2021).
  - AI-based segmentation validation for healthy individuals (SALIMI et al. 2025)
- **Interoperability**: Integration with PACS, RIS, DICOM standards.
- **Usability**: User interface, automation level, error-handling, and training needs.
- **Scalability and robustness**: Handling of large datasets, web-based/cloud vs. local performance.



Commercial/Clinically Available Software

Product (vendor)	Calculation models	Input data	Time-points	Segmentation & Registration	Regulation	Reporting & workflow integration	Validation references
3D-RD-S (Rapid Dosimetry)	Organ/tissue-level dosimetry	TAC/TIAC	Single, multi	Manual, semi-auto (web-based VOI management); Rigid registration using 3DSlicer	FDA 510(k) cleared (K191001), CE marked	Web-based reports, patient/project hierarchy, dose uncertainties; exportable results	Prideaux et al., Med Phys 2007. PMID: 17388154
Hermia Voxel Dosimetry (Hermes Medical Solutions)	Organ-level dosimetry; voxel S-values + fast MC dosimetry	SPECT/CT, PET/CT, PET/MR, planar, TIAC/TAC	Single, multi	Manual, semi-auto, ML-based segmentation; Rigid + deformable registration	FDA 510(k) cleared (K213123), CE marked	DVHs, absorbed dose maps, DICOM RT export; integrates with clinical records	Gear et al., EJNMMI Phys 2018. PMID: 30293172
PLANET® Dose (DOSIsoft)	Voxel S-values dosimetry	SPECT/CT, PET/CT, planar, TIAC	Single, multi	Manual, semi-auto; Rigid + deformable registration	FDA-approved for ^{90}Y; CE marked (EU MDR certified)	DVHs, organ dose reports, DICOM RT export; hospital workflow integration	Chiesa et al., EJNMMI Phys 2020. PMID: 32394307; Sjögreen-Gleisner et al., Med Phys 2019. PMID: 30809924
MIM SurePlan MRT (MIM / GE HealthCare)	Local deposition or voxel S-values dosimetry	SPECT/CT, PET/CT, planar, hybrid	Single, multi	Manual, semi-auto, AI/ML-assisted auto segmentation for organs and tumors; Rigid + deformable registration	FDA 510(k) cleared (K192328), CE marked	DVHs, dose maps, reporting tools, DICOM RT; integrates with oncology workflow	Jackson et al., Med Phys 2020. PMID: 32557562
Torch® / Voximetry (Voximetry)	GPU full MC voxel-based engine	SPECT/CT, PET/CT, planar	Single, multi	Manual, semi-auto, automated contour propagation; Rigid + deformable registration	Commercial product; clinical deployments	DVHs, voxel dose maps, DICOM export; workflow acceleration	Dewaraja et al., JNM 2021. PMID: 33688025; vendor validation white papers
QDOSE / QDOSE+ (Versant / Telix)	Organ-level dosimetry using S-values	SPECT/CT, PET/CT, planar, TAC, TIAC	Single, multi	Manual, semi-auto, automated organ segmentation; Rigid + deformable registration	FDA 510(k) cleared (K230844), CE-marked	DVHs, dose maps, DICOM RT export; PACS/TPS integration	Tran-Gia et al., EJNMMI Phys 2021. PMID: 34196190

HTA framework

Clinical Effectiveness

- **Evidence synthesis**:
  - Systematic review of clinical studies linking dosimetry-guided treatment to improved outcomes (e.g., tumor control probability, reduced toxicity).
    - LAWHN-HEATH et al., Lancet Oncology (2022)
- **Endpoints**:
  - Patient outcomes (survival, response rates, toxicity reduction).
  - Surrogate outcomes (dose–response correlation, predictive biomarkers).
- **Comparison with non-dosimetry-based therapies**:
  - Incremental benefit of personalized dosimetry.
    - DOSISPHERE-01 ^{90}Y clinical trial – The Lancet (2021)
    - ^{177}Lu-DOTATATE clinical trial – JNM (2025)

HTA framework

Safety

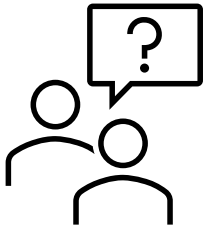
- **Direct risks**: Potential for incorrect dose estimation due to software errors, segmentation or registration mistakes, or user input issues.
- **Indirect risks**: Misinterpretation of results leading to under- or over-treatment.
- **Cybersecurity**: Data protection, compliance with GDPR(EU)/HIPAA(US).

Economic Evaluation

- **Cost-effectiveness analysis**: Incremental cost gained when using personalized dosimetry.
- **Cost-benefit or budget impact analysis**:
  - Software acquisition, licensing, and maintenance costs.
  - Training and workflow changes.
  - Savings from avoided toxicities or improved treatment outcomes.

SÁNCHEZ-ARTUÑEDO et al. (2024) JACMP

HTA framework



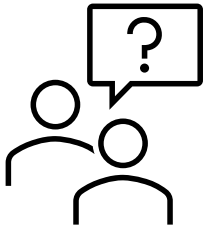
Organizational Impact

- **Workflow integration**: Time required for image processing, reporting, and clinician acceptance.
- **Resource requirements**: IT infrastructure, additional staff training, quality assurance procedures.
- **Adoption barriers**: Complexity, regulatory approval, interoperability issues.

Legal, Ethical, and Social Implications

- **Legal/regulatory**: CE marking, FDA clearance, compliance with IEC standards.
- **Ethical**: Equitable access to personalized dosimetry; implications of not using available precision tools.
- **Social**: Patient perception of personalized treatment; impact on trust and shared decision-making.

HTA framework



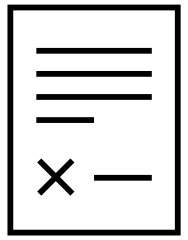
Evidence Appraisal and Uncertainty

- **Strength of evidence**: Randomized controlled trials, observational studies, phantom validation, expert consensus.
- **Uncertainty assessment**: Sensitivity analyses in economic models.
- **Research gaps**: Need for prospective trials, multicenter validation, and real-world performance monitoring.

Recommendations and Decision-Making

- **HTA report output**: Balanced summary of clinical benefit, cost-effectiveness, risks, and organizational feasibility.
- **Guidance**: Whether the dosimetry software should be recommended, conditionally approved (e.g., in specialized centers), or further studied.

HTA framework



- **ROMA (Research-Oriented Managed Access)** framework provides contractual agreements for technologies that face significant uncertainty regarding their effectiveness and/or cost-effectiveness.
- Contract should specify:
  - research protocol to be followed;
  - research duration;
  - data sources to be used, including routinely collected data.
- Evidence produced through ROMA is used to reevaluate the technology and guide adoption decisions, while enabling managed market access.

KIRWIN et al. (2022) Value Health

Radiotheranostics Software Features

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MANDATORY	RECOMMENDED	OPTIONAL
DICOM data input	Flexible Input	Quantitative Reconstruction
Image Calibration Factor	Image Registration and Segmentation	Implementation of Blood-Based Dosimetry
Administered Activity and Time of Administration	Workflows and Saving of Intermediate Results	Standardized Output
Image Segmentation	PVE Correction	Surrogate Nuclide Dosimetry
Time-Integrated Activity Modeling	Multiple Absorbed Dose Calculation	Patient Clinical History and Absorbed Dose Tracking
Absorbed Dose Calculation	Error Propagation and Uncertainty Analysis	Customer Support
Dose–Volume Histograms		
DICOM Saving		
Saving Output Data		
Saving Output Reports		

KESNER et al. (2025) JNM

Conclusions

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- **No benchmarking process** exists to compare radiotheranostics software, underscoring the need for reliable tools to systematically evaluate solutions and their versions.
- Personalized dosimetry for radiotheranostics is **not routinely performed** in many nuclear medicine departments, despite the availability of **regulatory-cleared software solutions**.
- To support standardized radiotheranostics software assessment, the development, deployment, and accessibility of **open benchmark datasets** should be actively promoted.

Conclusions

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- The **variability in radiotheranostics software** solutions, particularly in their calculation algorithms and compliance with standardized protocols, highlights the need for **better harmonization**.
- We should establish mechanisms for reassessing medical software solutions in response to changes in versions, particularly those involving **AI-based solutions**.
- **Contractual agreements** for radiotheranostics software solutions should specify a testing protocol period, the duration of the testing phase, and the data sources to be used, including routinely collected data.