Department of Medical Physics
UNIVERSITY OF WISCONSIN – MADISON
SCHOOL OF MEDICINE AND PUBLIC HEALTH

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RADIOLOGICAL ENGINEERING
& DESIGN LABORATORY

Building Clinical Infrastructure for Radiotheranostics: Insights from a Health Technology Assessment Framework

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Conflict of Interest

I am a Co-Founder of Voximetry, Inc a nuclear medicine dosimetry company located in Middleton, WI. I have financial interest in the company.

Health Technology Assessment

Health Technology Assessment (HTA) is a systematic, multidisciplinary process that evaluates the **VALUE** of health technologies across their lifecycle (beyond a clinical trial).

- **Clinical effectiveness & safety** – How well a technology works and whether it is safe
- **Economic & financial implications** – Cost-effectiveness, investment vs. return
- **Patient/stakeholder impacts** – Impact on patients, caregivers, and relevant stakeholders.
- **Organizational impacts** – Effects on health systems and the organization
- **Legal aspects** – Evaluates any legal implications of using the technology

Technology Value Chain

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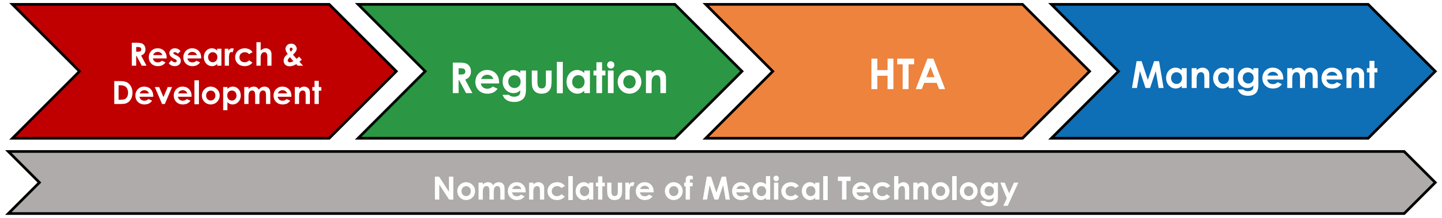

Characteristics	Health technology regulation	Health technology assessment	Health technology management
Perspective	Market access: considerations include quality, safety, performance and efficacy	Population-level: considerations include efficacy, relative effectiveness, safety, patient-relevant outcomes, appropriateness (including ethics, social and legal issues) and accessibility	Local-level health facilities: considerations include needs analysis, procurement, affordability, training and alternative technologies towards quality of care
Requirement	Mandatory	National recommendation on complex technologies	Local implementation of recommended technologies
Role	Prevent harm	Maximize clinical and cost-effectiveness, value-based decision-making	Management across the lifecycle of the device, from adoption to decommissioning to enhance appropriate and safe use

Centralized National HTA Programs

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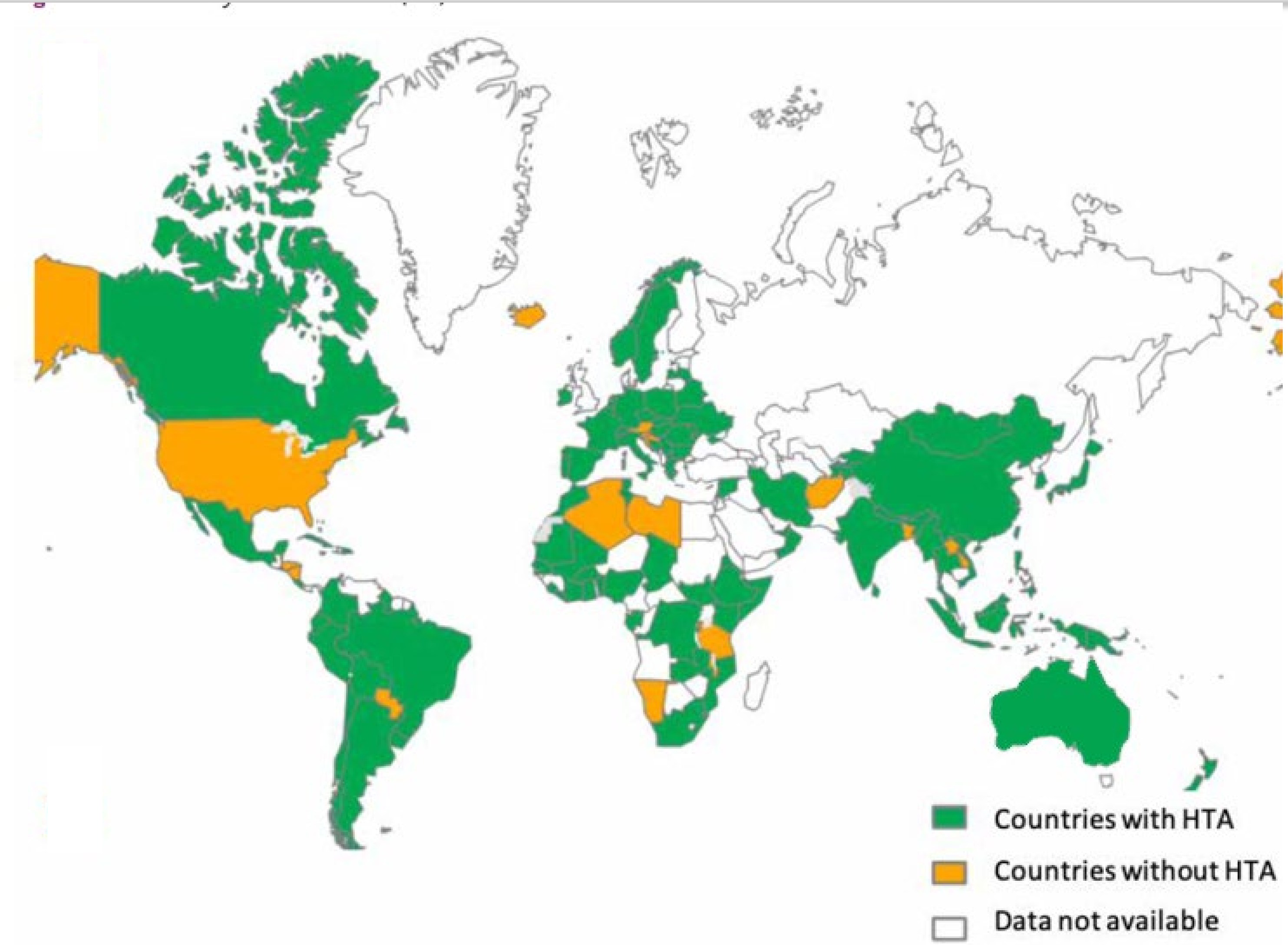

What is Value?

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Benefits

- Effectiveness: Improved survival
- Quality of Life: Enhanced health-related QoL'
- Safety: Fewer and less severe adverse events
- Societal & Economic Benefits:
  - ❑ Reduced caregiver burden
  - ❑ Increased workforce productivity
  - ❑ Wider community economic gains

Costs

- Direct:
  - ❑ Technology price (drug, device, etc.)
  - ❑ Implementation (training, IT, infrastructure)
  - ❑ Downstream care and follow-up
- Indirect & Societal:
  - ❑ Informal care burden/time costs
  - ❑ Productivity loss for patients & caregivers

Health Technology Assessment

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Incremental Cost Effectiveness Ratio:

$$\text{ICER} = \frac{C_1 - C_2}{E_1 - E_2} = \frac{\Delta C}{\Delta E}$$

$C_{1,2}$ =cost of technology and comparison

$E_{1,2}$ =effect of technology and comparison*

*Typically measured in quality adjusted life years (QALY)

QALY = Yrs added x QOL weight

Net Health Benefit:

$$NHB = \lambda \Delta E - \Delta C$$

λ: cost effectiveness threshold or max the decision maker is willing to pay for a unit of effect

$50K per QALY

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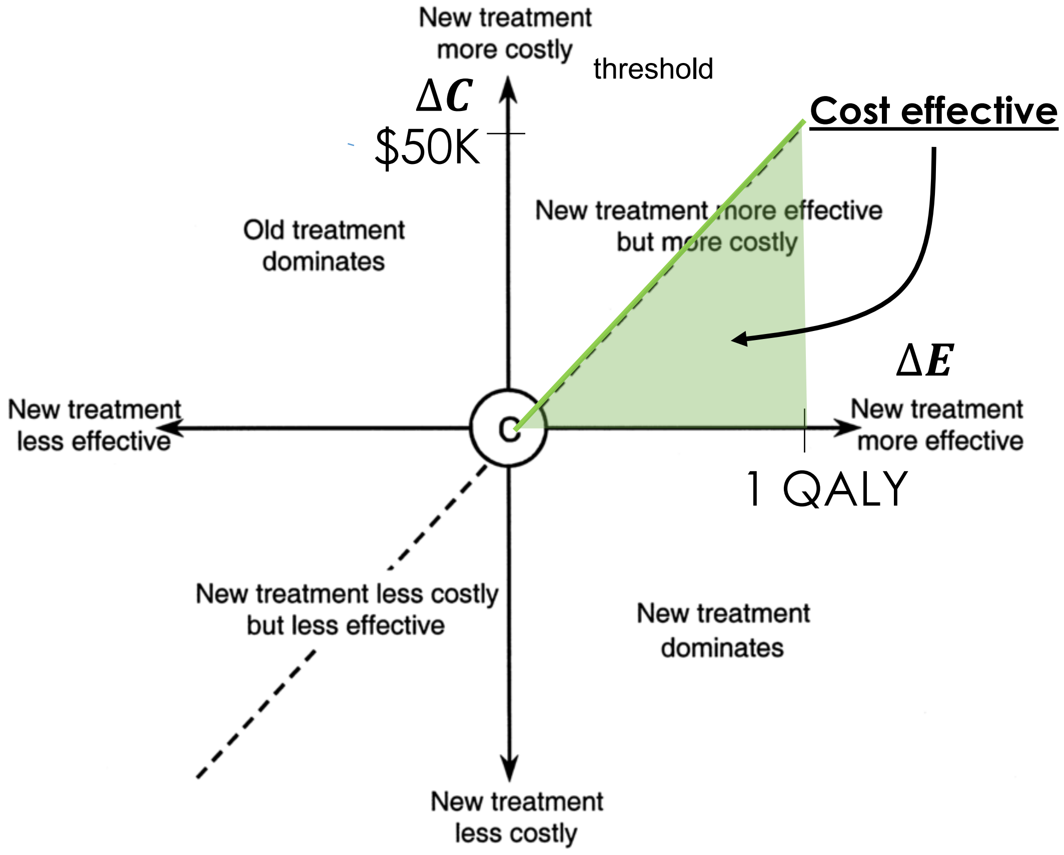
Incremental net monetary benefit:

$$\lambda \Delta E - \Delta C > 0$$

Incremental net health effect:

$$\Delta E - \frac{\Delta C}{\lambda} > 0$$



Health Technology Assessment

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Consider three drugs currently in the market for metastatic prostate cancer. Drug A yields 8 additional QALYs, Drug B yields 15 additional QALYs, and Drug C yields 5 additional QALYs, each compared to an appropriate standard-of-care comparator. The incremental costs are $150,000 for Drug A, $300,000 for Drug B, and $120,000 for Drug C. The target populations are 15 patients for Drug A, 20 patients for Drug B, and 10 patients for Drug C. The allocated budget for prostate cancer is $3,000,000.

Intervention	# of relevant patients	ΔC	ΔE	ICER = ΔC/ΔE	Total incremental effectiveness (# of relevant patients × ΔE)	Total incremental cost (# of relevant patients × ΔC)	Budget impact in current period	Funded (%)
A	15	150,000	8	18,750	120	2,250,000	1,000,000	Yes (100%)
B	20	300,000	15	20,000	300	6,000,000	1,800,000	Yes (100%)
C	10	120,000	5	24,000	50	1,200,000	500,000	Yes (40%)
						A + B + C =	∑ 3,300,000	

Highest ICER

%Funded Cut

What happens if a “blockbuster” radiopharmaceutical is introduced into the market?

Health Technology Assessment

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When a new intervention (Drug D, a radiopharmaceutical) is introduced and a decision maker considers reimbursement, its ICER must be compared with the current ICER threshold—here, the ICER of worst performing drug, Drug C ($ICER_{last}$). Suppose Drug D treats 12 patients, has an incremental cost of $130,000, and an incremental effect of 6 QALYs. Its budget impact in the current period is $700,000.

Intervention	# of relevant patients	ΔC	ΔE	ICER = ΔC/ΔE	Total incremental effectiveness (# of relevant patients × ΔE)	Total incremental cost (# of relevant patients × ΔC)	Budget impact in the budget period	Funded (%)
A	15	200,000	8	18,750	120	2,250,000	1,000,000	Yes (100%)
B	20	400,000	15	20,000	300	6,000,000	1,800,000	Yes (100%)
C	10	200,000	5	24,000	50	1,200,000	500,000	No
				>		A + B + C =	∑ 3,300,000	
D	12	130,000	6	21,667	72	1,560,000	700,000	Yes (29%)
						A + B + D =	∑ 3,500,000	

divested (→ C)

Theranostics Ecosystem

BAYER

NOVARTIS

Radiopharmaceuticals

Supply Chain

- **Isotopes**: SHINE, NorthStar Medical Radioisotopes, IONETIX, Eckert & Ziegler, LANTHEUS
- **Imaging**: GE, SIEMENS, PHILIPS, SPECTRUM Dynamics Medical
- **Radiation Safety**: COMECER
- **Dosimetry**: MIM Software, DOSIsoft, Hermes Medical Solutions, VOXIMETRY

"Enablers"

Theranostics Ecosystem

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PeptiDream | Genentech (A Member of the Roche Group) | POINT Biopharma | Lilly | Bayer | Novartis | RayzeBio | Bristol Myers Squibb

Radiopharmaceuticals

Supply Chain — **Isotopes** | **Imaging** | **Radiation Safety** | **Dosimetry** — "Enablers"

- **Isotopes:** SHINE; NorthStar Medical Radioisotopes; IONETIX; Eckert & Ziegler; LANTHEUS
- **Imaging:** GE; SIEMENS; PHILIPS; SPECTRUM Dynamics Medical
- **Radiation Safety:** COMECER
- **Dosimetry:** MIM Software; DOSIsoft; HERMES MEDICAL SOLUTIONS; VOXIMETRY

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Theranostics Ecosystem

PeptiDream
Genentech — A Member of the Roche Group
POINT Biopharma
Lilly
Bayer
Novartis
RayzeBio
Bristol Myers Squibb

"Enabler"

Supply Chain | Isotope

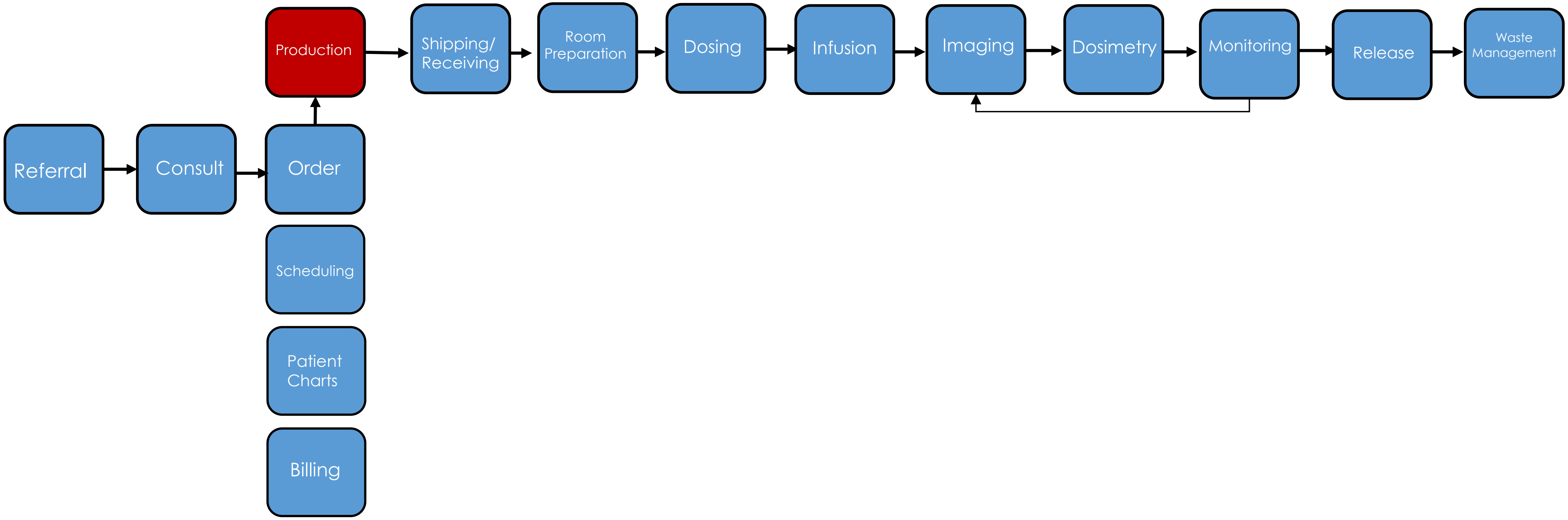
osimetry | "Enablers"

Perspective Therapeutics
Seagen
Telix
Convergent Therapeutics
Ratio Therapeutics
RadioMedix — Innovating Theranostics
Clarity Pharmaceuticals
Fusion
Radionetics Oncology
oranomed
Lantheus
3B Pharmaceuticals
Ablaze
Blue Earth Therapeutics — A Bracco Company
ArtBio
Actinium Pharmaceuticals, Inc.
RAD Radiopharm Theranostics
mariana Oncology
Aktis Oncology
AdvanCell
OncoTherapy Science, Inc.
alpha9 Oncology
itm
Precision Molecular
Ariceum
Abdera Therapeutics
Cellectar Biosciences
Primo
Nucleus RadioPharma
Molecular Partners
RAD Radiopharm Theranostics
Archeus
Precirix
Curium — Life Forward

SHINE
NorthStar Medical Radioisotopes
Eckert & Ziegler
Lantheus

mim Software
DSI Xsoft
Hermes Medical Solutions
Voximetry

Clinical Infrastructure



Clinical Infrastructure

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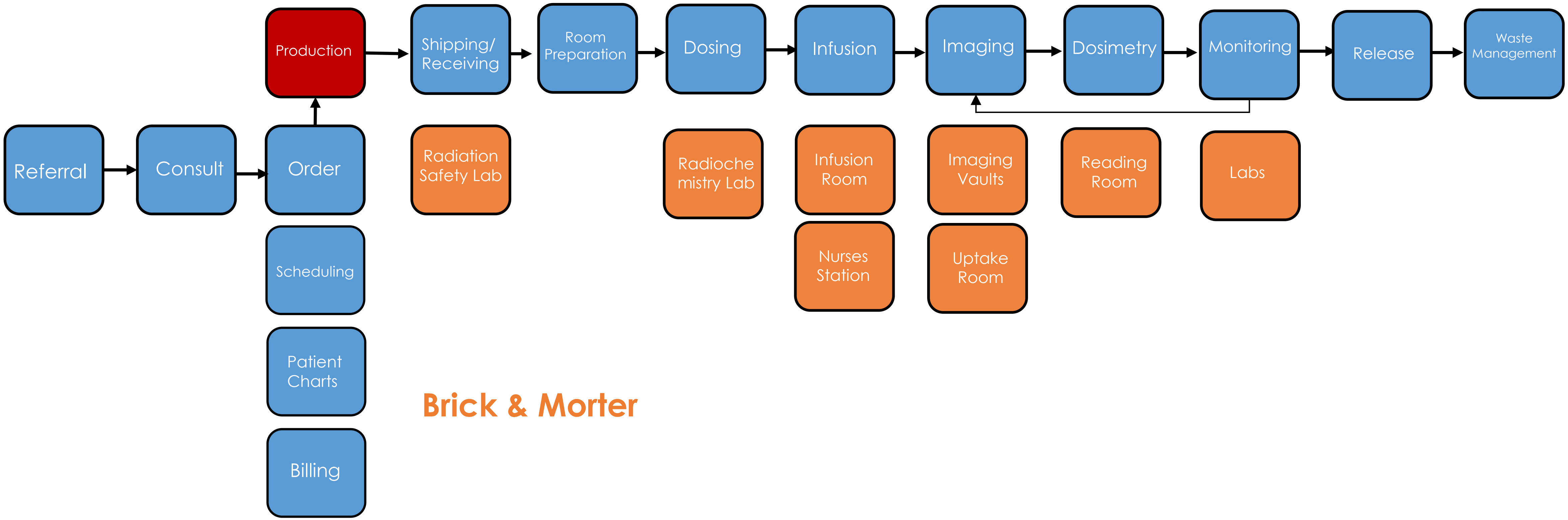
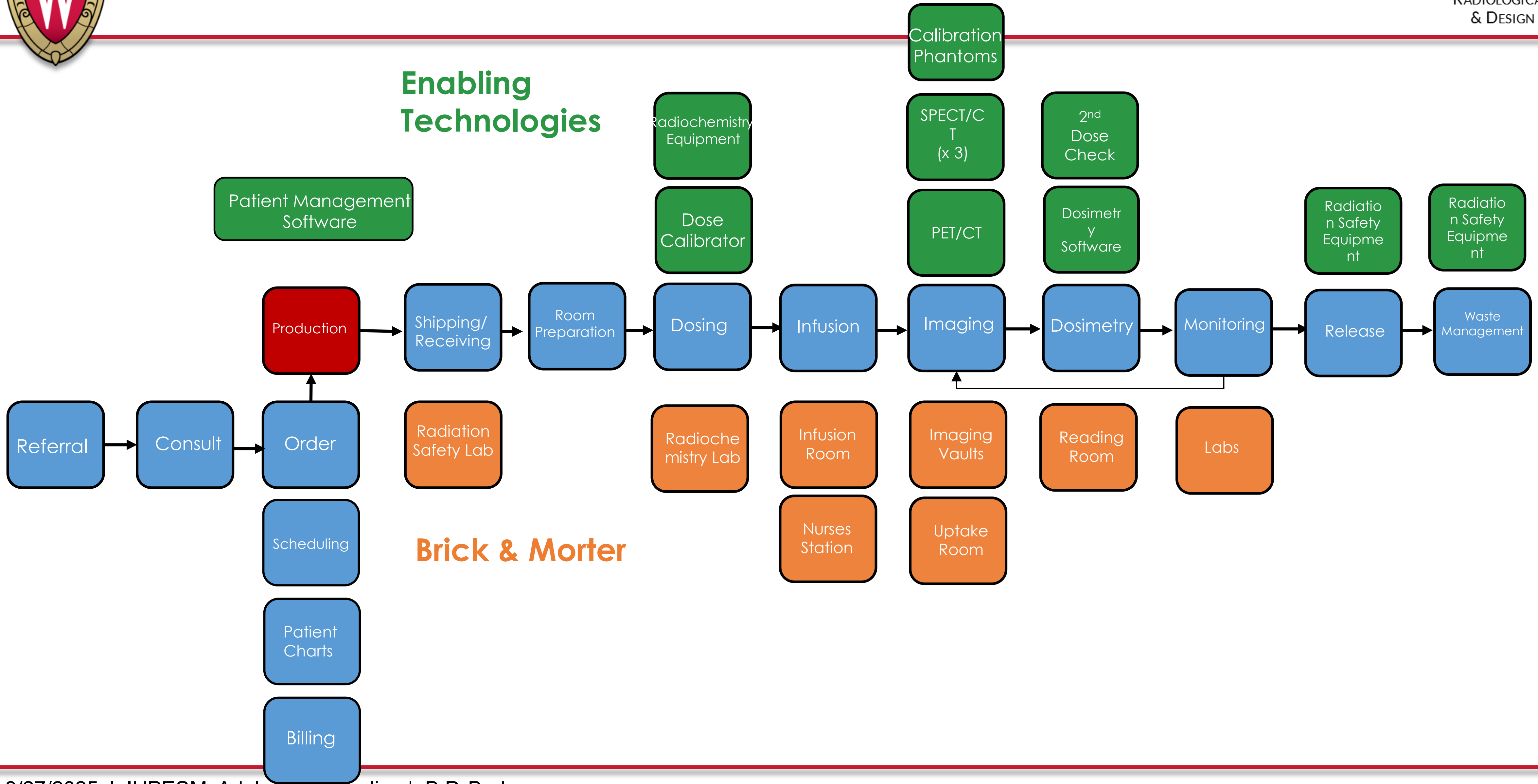
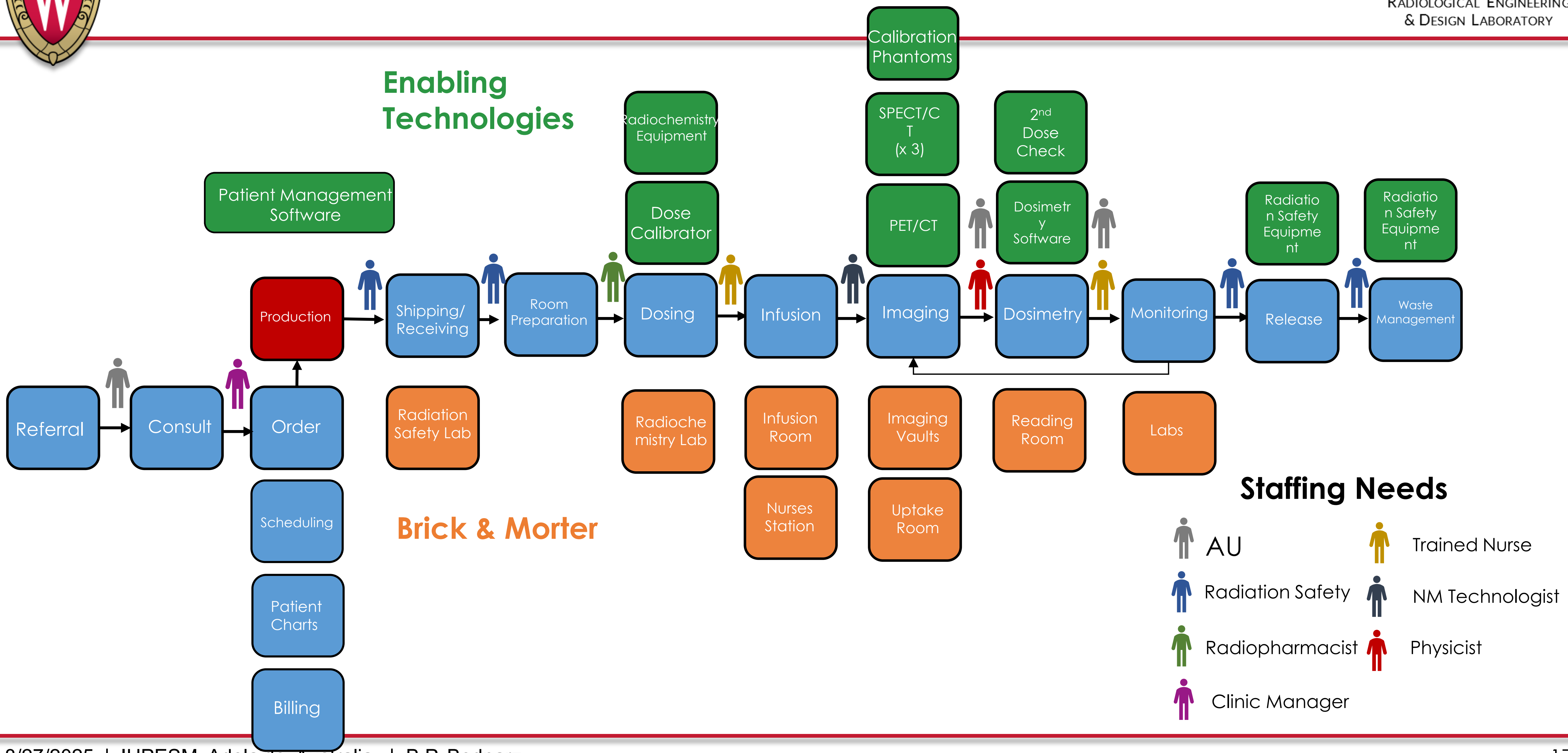


Clinical Infrastructure



Clinical Infrastructure



Transarterial Radioembolization (TARE)

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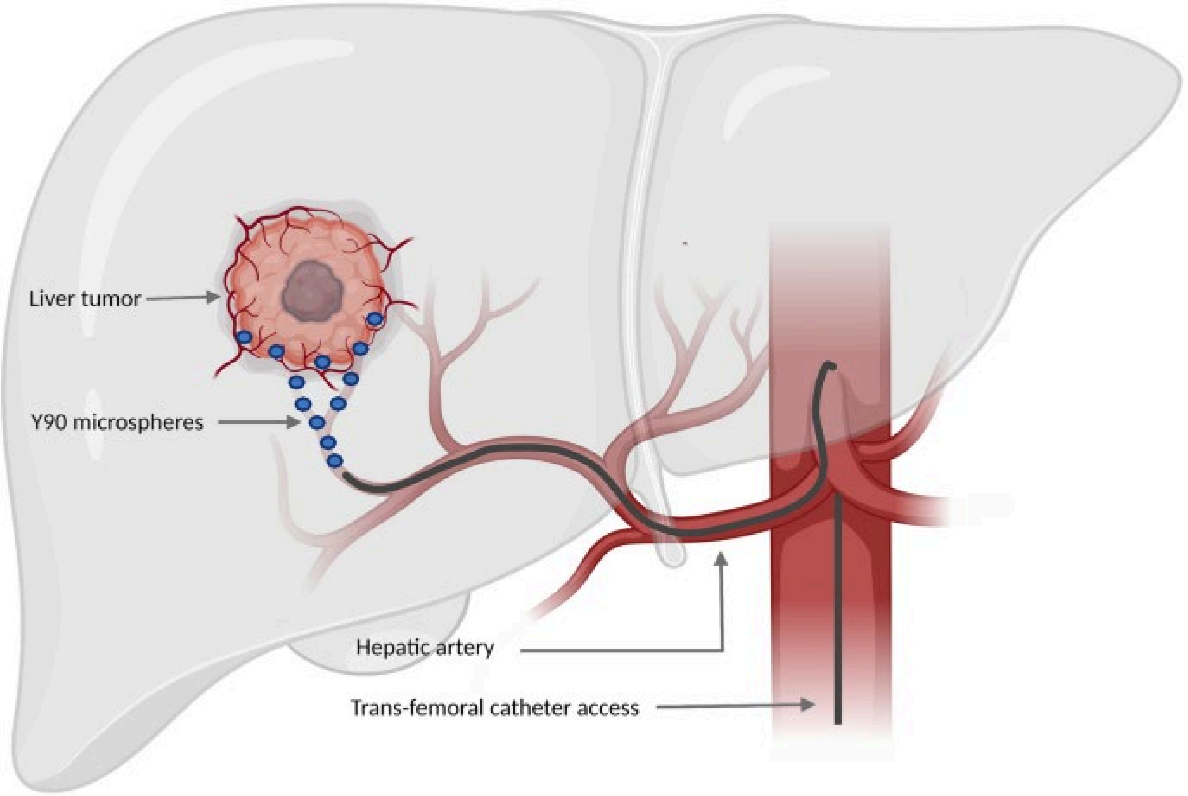
SARAH Trial: Phase III clinical study comparing ^{90}Y SIRT to sorafenib in patients with advanced HCC who were not eligible for curative resection or local ablation.

DOSISPHERE-01 Trial: Phase II randomized study that evaluate the benefit of using personalized dosimetry versus standard dosimetry for ^{90}Y TARE.



*Sorafenib (kinase-inhibitor) has standard of care for HCC treatment.

Procedural Costs

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	Calculation method	Valuation
Human Resources	Cost of staff = Σ (hourly personnel cost x time of attendance x number of people)	The hourly personnel cost is calculated on the basis of the salary and charges for the average grade of each type of staff (Table S1.2). We consider that a person worked 1607 hours during the year.
Consumables	Cost of consumables = Σ (purchase price of a consumable x number of consumables)	The unit prices of consumables have been valued at their purchase price (Table S1.3).
Intervention room (including Imaging)	Cost of the intervention room = room cost per hour x room occupancy	The cost of the radiology room comes from the 2012 cost accounting of Beaujon hospital. We consider that during this year, the intervention room operated 8 hours a day for 250 working days.
Initial hospital stay	Cost of hospital stay = (cost of the stay for the DRG / average length of stay observed in DRG) x Length of Stay	The cost of the stay is valued using DRGs from the national production cost study (ENCC) 2015.
Sorafenib	Cost of sorafenib= Σ (purchase price x dose)	The unit prices of drugs have been valued at their purchase price (Table S1.3).
Follow-up hospitalizations (adverse event)	hospitalizations cost = ∑ (GHS tariff)	The cost of the hospitalizations is valued using GHS cost (ATIH 2015).
Second and third line treatments admission	hospitalizations cost = ∑ (GHS tariff)	The cost of the hospitalizations is valued using GHS cost (ATIH 2015).
Second and third line oral treatments	Cost of drugs = Σ (purchase price of a drug x dose)	The unit prices of drugs have been valued at their purchase price (Table S1.3).

TARE Cost-Benefit Analysis

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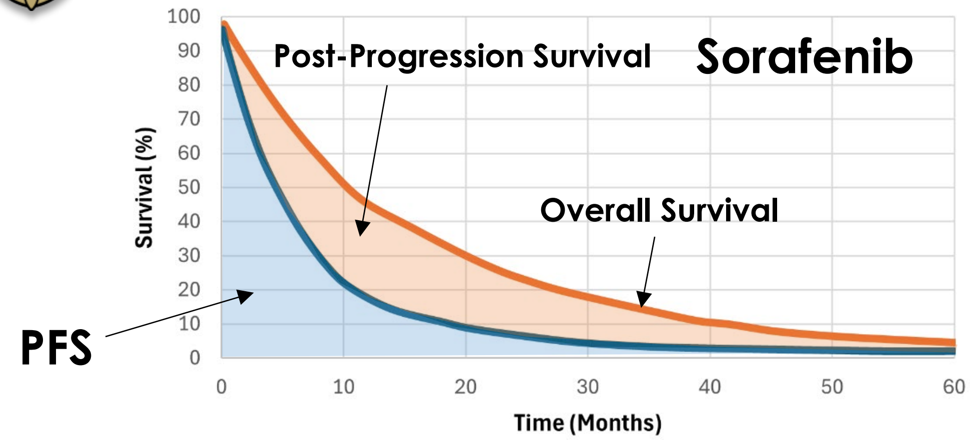

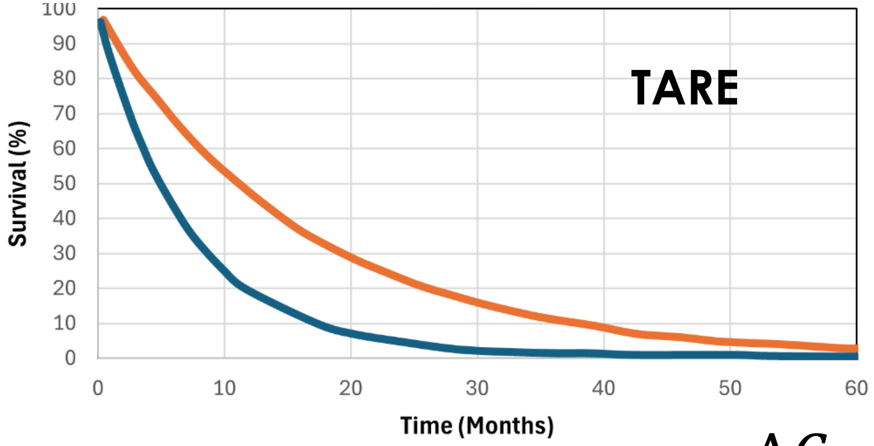

CBA Model

	TARE	Sorafenib
Quality of Life		
QALYs	0.803	0.797
Procedural Costs (USD)		
Initial workup	6500	0
Initial radioembolization	20000	0
Imaging	3000	0
Additional Radioembolization	7000	0
Sorafenib	0	20000
Follow-up Costs (USD)		
Second-line treatments	4000	1300
Third-line treatments	800	400
Admission for SAEs	3200	3000
Other Admissions	2200	1200
Total Cost Per Patient	**46700**	**25900**

$$\text{ICER} = \frac{\Delta C}{\Delta E} = \frac{46700 - 25900}{0.803 - 0.797} \approx 3.5M\ u/QALY$$

Zarca K. et al Clin Ther. 2021 Jul;43(7):1201-1212.

TARE Cost-Benefit Analysis

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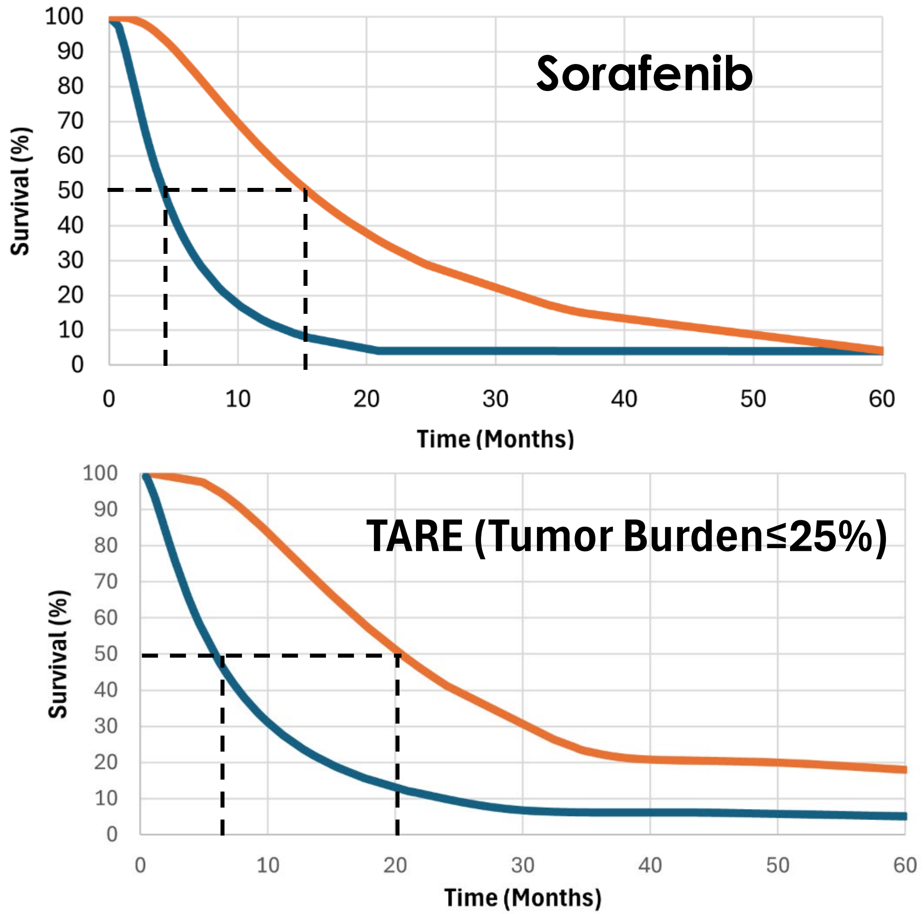

CBA Model

	TARE	Sorafenib	TARE (TB≤25%)
Quality of Life			
QALYs – 5 yr	0.80	0.79	1.00
Procedural Costs (USD)			
Initial workup	6500	0	
Initial radioembolization	20000	0	
Imaging	3000	0	
Additional Radioembolization	7000	0	
Sorafenib	0	20000	
Follow-up Costs (USD)			
Second-line treatments	4000	1300	
Third-line treatments	800	400	
Admission for SAEs	3200	3000	
Other Admissions	2200	1200	
Total Cost Per Patient	46700	25900	29500

$$\text{ICER} = \frac{\Delta C}{\Delta E} = \frac{29500 - 25900}{1.00 - 0.79} \approx 17400\ u/QALY$$

Muszbek N et al Future Oncol. 2021 Mar;17(9):1055-1068

TARE Cost-Benefit Analysis

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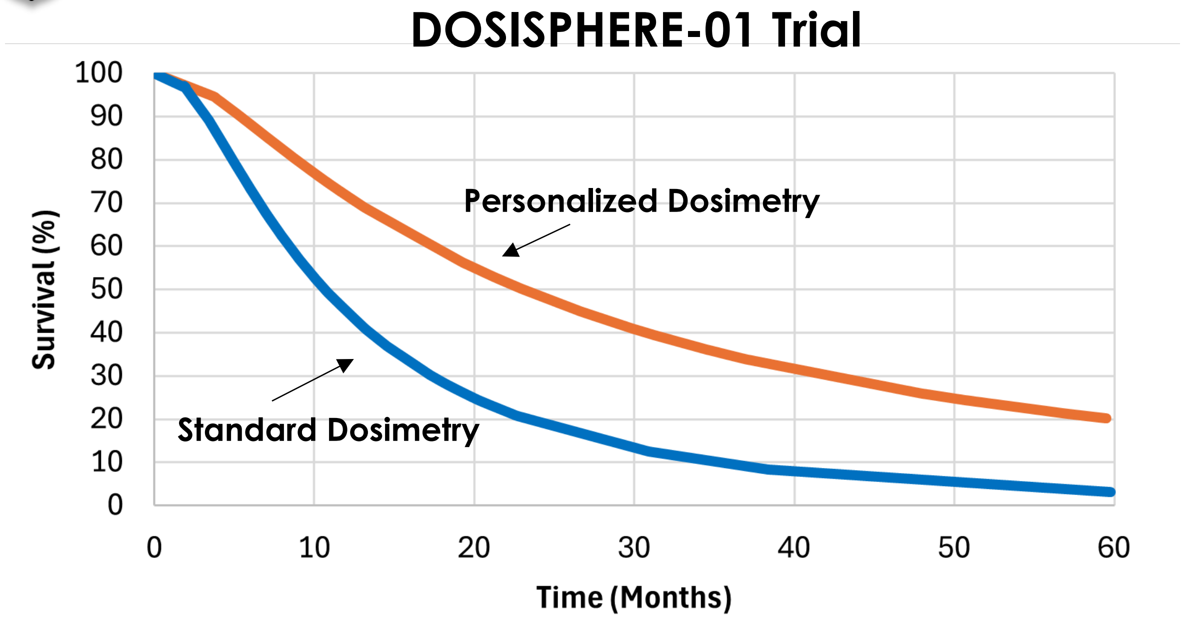

CBA Model

	TARE	Sorafenib	TARE (TB≤25%)	TARE (Pers. Dose)
Quality of Life				
QALYs – 5 yr	0.80	0.79	1.00	1.30
Procedural Costs (USD)				
Initial workup	6500	0		
Initial radioembolization	20000	0		
Imaging	3000	0		
Additional Radioembolization	7000	0		
Sorafenib	0	20000		
Follow-up Costs (USD)				
Second-line treatments	4000	1300		
Third-line treatments	800	400		
Admission for SAEs	3200	3000		
Other Admissions	2200	1200		
Total Cost Per Patient	46700	25900	29500	30000

$$\text{ICER} = \frac{\Delta C}{\Delta E} = \frac{30000 - 25900}{1.30 - 1.0} \approx 14000\, u/QALY$$

Rognoni C. et al Front Oncol. 2022 Aug 29;12:920073.

Concluding Remarks

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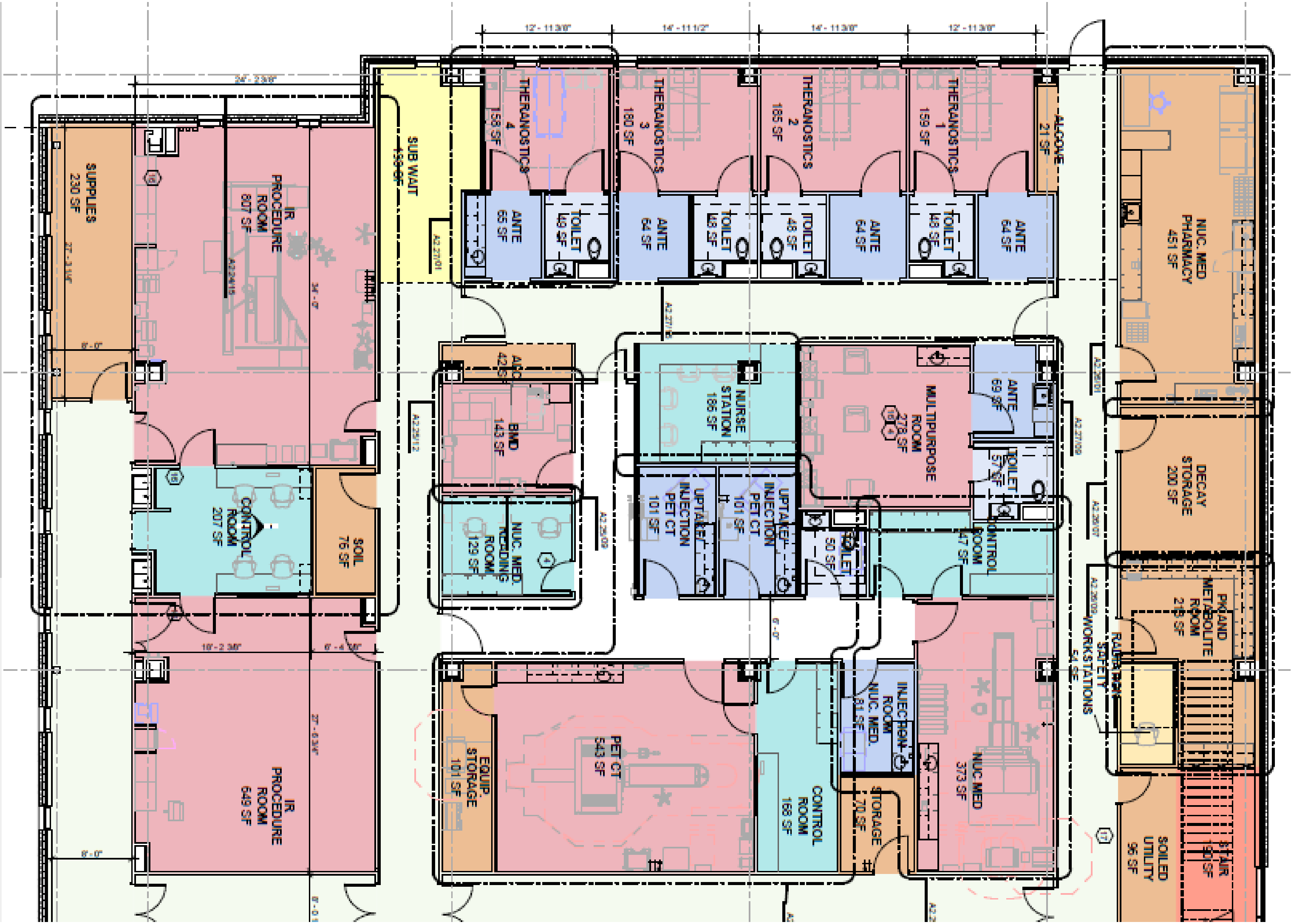
- Health Technology Assessment (HTA) provides a structured way to evaluate clinical effectiveness, safety, cost-effectiveness, and system impact for emerging radiotheranostics.
- Successful adoption of radiotheranostics requires integrated clinical infrastructure — physical facilities, enabling technologies, trained staff, and coordinated processes across imaging, dosimetry, pharmacy, and patient care.
- Value-based frameworks (e.g., ICER, net health benefit) help inform investment from health centers, particularly as novel radiopharmaceuticals and enabling technologies enter the market.
- Collaboration across academic centers, health systems, industry, and regulators is essential to scale safe, cost-effective, and patient-centered theranostics.


SUPPLIES
230 SF
IR
PROCEDURE
ROOM
607 SF
SUB WAIT
THERANOSTICS
4
158 SF
THERANOSTICS
3
180 SF
THERANOSTICS
2
185 SF
THERANOSTICS
1
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ALCOVE
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ANTE
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TOILET
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NUC. MED
PHARMACY
451 SF
CONTROL
ROOM
207 SF
SOIL
76 SF
ACC
42 SF
BMD
143 SF
NUC. MED
READING
ROOM
129 SF
NURSE
STATION
186 SF
UPTAKE/
INJECTION
PET CT
101 SF
UPTAKE/
INJECTION
PET CT
101 SF
MULTIPURPOSE
ROOM
278 SF
ANTE
69 SF
TOILET
57 SF
TOILET
50 SF
CONTROL
ROOM
147 SF
DECAY
STORAGE
200 SF
PK AND
METABOLITE
ROOM
218 SF
RADIATION
SAFETY
WORKSTATIONS
54 SF
IR
PROCEDURE
ROOM
649 SF
EQUIP.
STORAGE
101 SF
PET CT
543 SF
CONTROL
ROOM
168 SF
NUC. MED.
INJECTION
ROOM
81 SF
STORAGE
70 SF
NUC MED
373 SF
SOILED
UTILITY
96 SF
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Acknowledgements

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Thank You!

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