The Use of Nuclear Imaging in the Workup and Management of a Renal Mass

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I have no disclosures

Objectives:

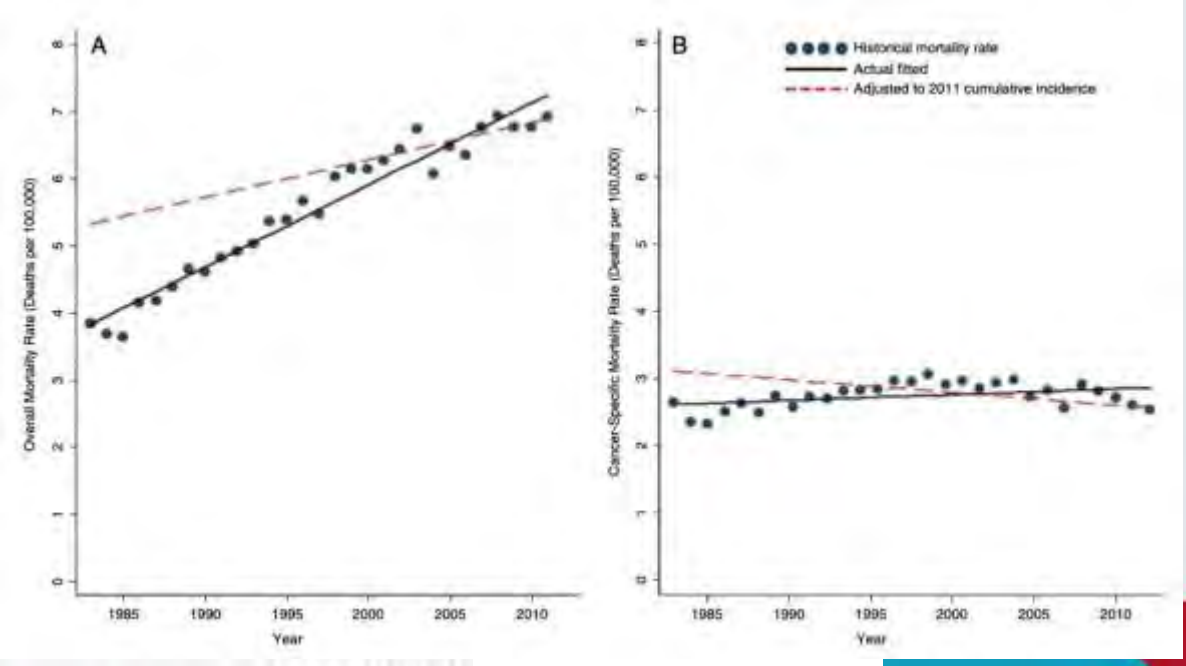
- Discuss the current workup strategy for newly diagnosed small renal mass
- Review the current state of use of nuclear imaging in the workup and management of small renal masses
- Discuss future direction to improve imaging accuracy

Increasing Incidence of Kidney Cancer

- Rise of cross-sectional imaging

  → Rise in kidney tumors

- Stage migration toward localized disease
- Mortality = Unchanged



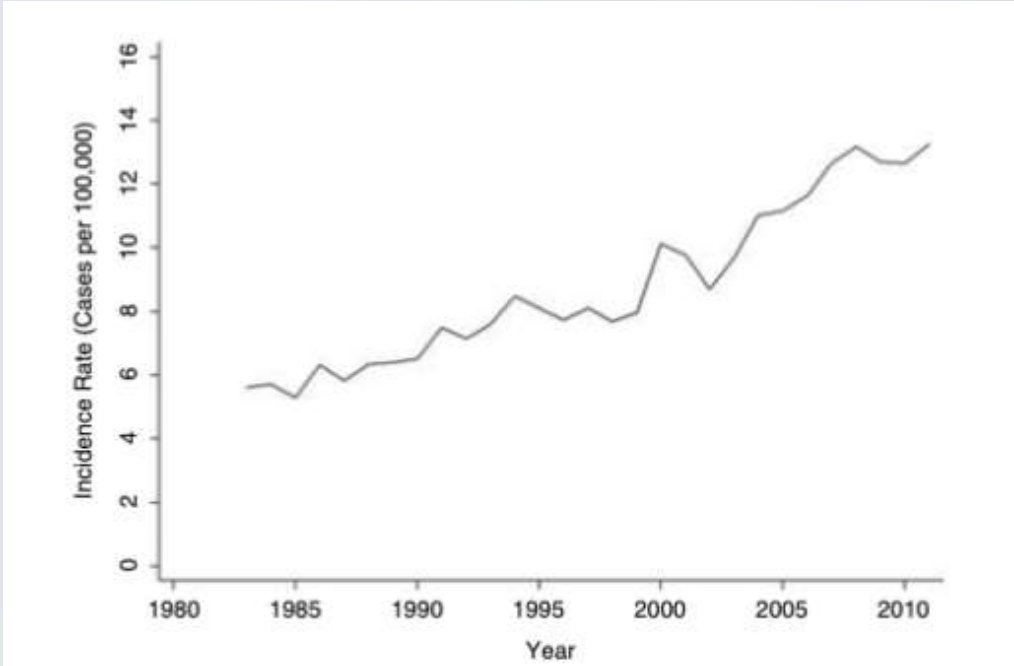


FIGURE 1. Age-adjusted kidney cancer incidence has uniformly increased across age categories over the study period of 1983–2011.

Smaldone et al. Understanding Treatment Disconnect and Mortality Trends in Renal Cell Carcinoma Using Tumor Registry Data. Published online October 10, 2016:1-7.

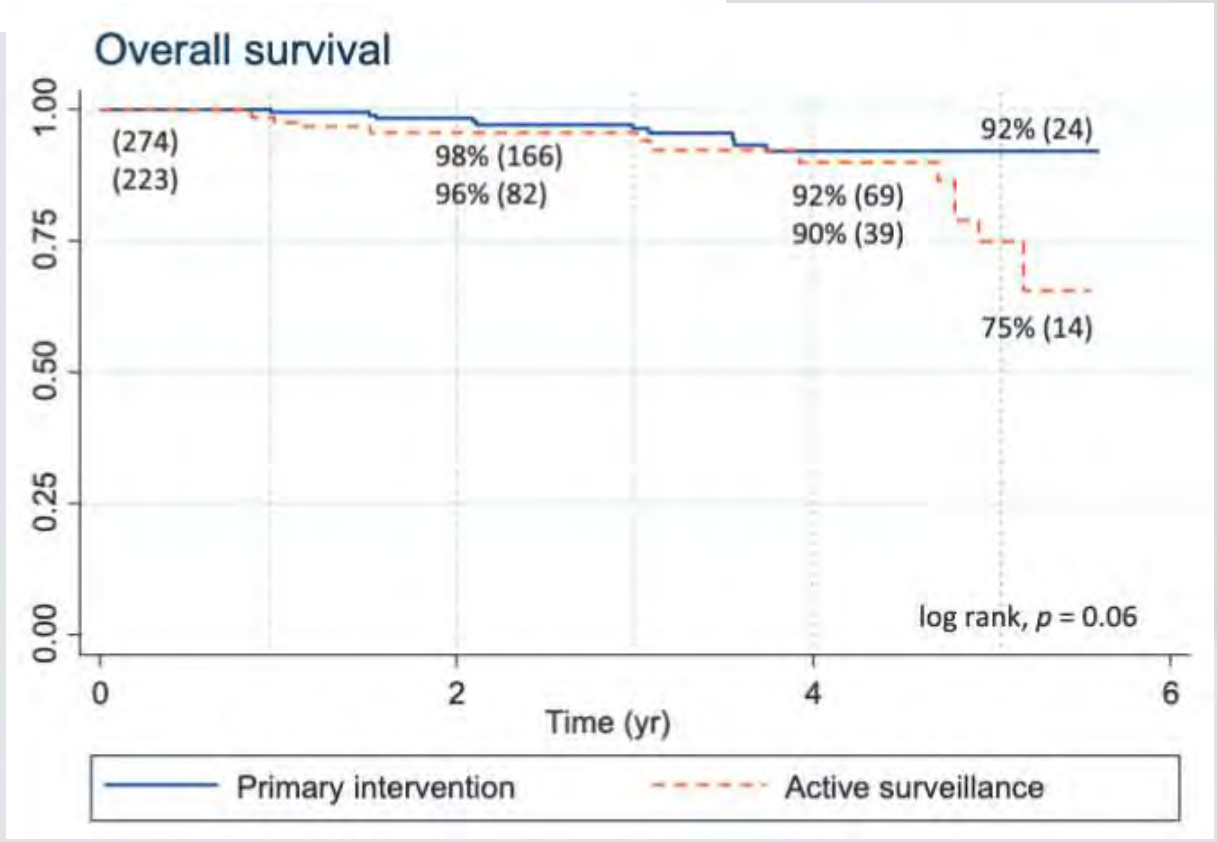
Change in Management Landscape

Five-year Analysis of a Multi-institutional Prospective Clinical Trial of Delayed Intervention and Surveillance for Small Renal Masses: The DISSRM Registry

- CSS: 99% in PI arm and 100% in AS arm

Parameter	Patients
Progression (active surveillance patients only; $n = 36$, 49 events) [a]	
Growth rate >0.5 cm/yr	34
Greatest tumor diameter >4.0 cm	2
Development of distant metastases	0
Crossover to delayed intervention	21
Recurrence (intervention patients only; $n = 11$)	
Local: at the resection site for partial nephrectomy	0
Metachronous: a new lesion within either kidney at a site distant to the original tumor	5
Distant: recurrence outside the kidney	2
Persistence: persistent enhancement following ablative treatment	2

[a] A patient can experience multiple progressions while on active surveillance. For instance, a single patient may progress by growth rate, exceed a tumor diameter of 4 cm, and undergo delayed intervention at a single time point. Alternatively, a patient's tumor may grow at >0.5 cm/yr on three separate occasions and also be considered as having three events during follow-up.



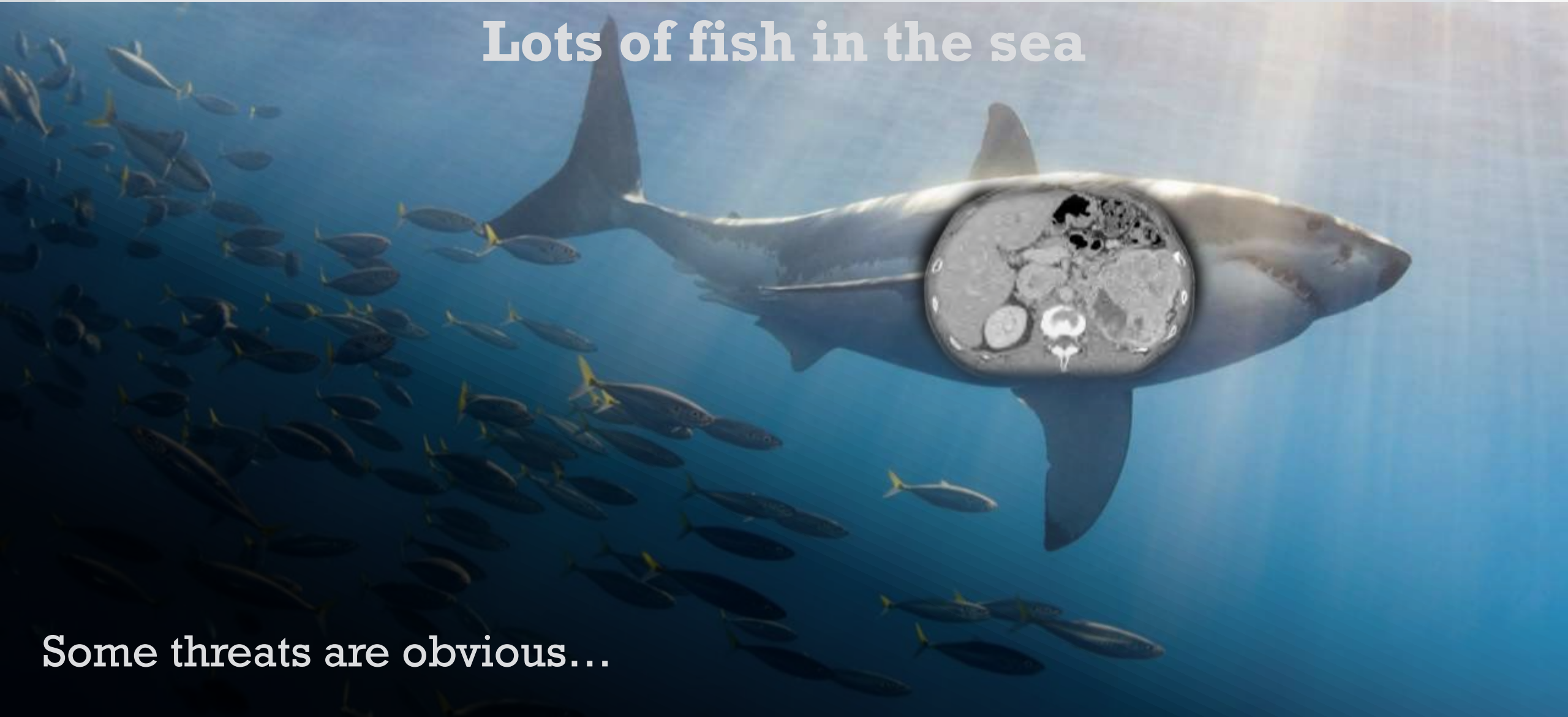
Pierorazio PM, Johnson MH, Ball MW, et al. Five-year Analysis of a Multi-institutional Prospective Clinical Trial of Delayed Intervention and Surveillance for Small Renal Masses: The DISSRM Registry. *Eur Urol*. 2015;68(3):408-415.

Limits of Cross-sectional Imaging: cT1a Benign Resection Rate

Harsh Reality:

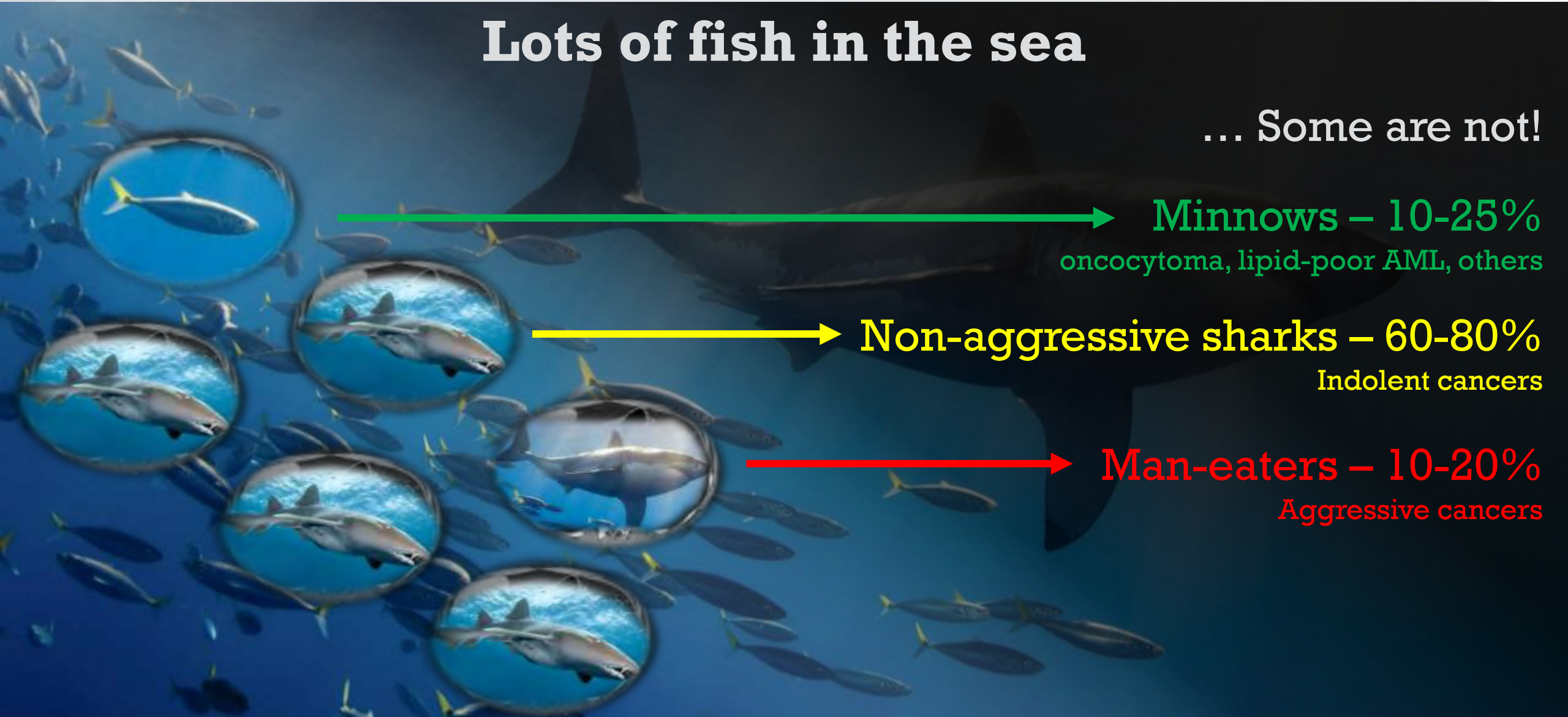
10-15% of Surgeries for SRM = Overtreatment

Lots of fish in the sea



Some threats are obvious…

Lots of fish in the sea



… Some are not!

Minnows – 10-25%

oncocytoma, lipid-poor AML, others

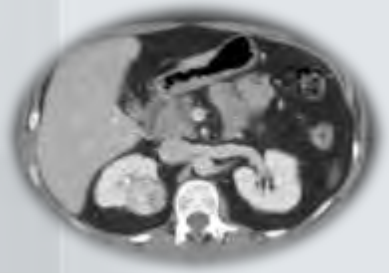
Non-aggressive sharks – 60-80%

Indolent cancers

Man-eaters – 10-20%

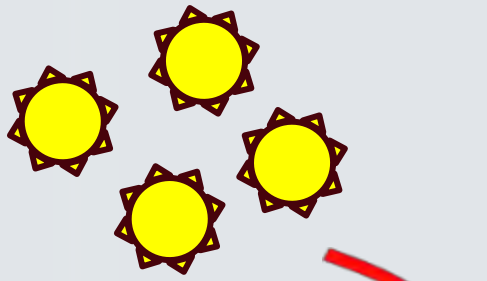
Aggressive cancers

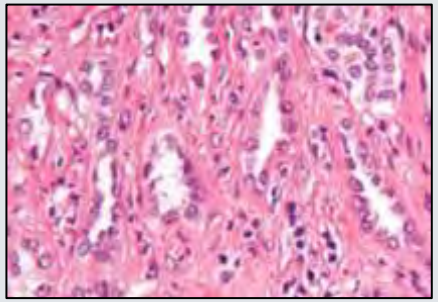
How can we tell which is what?

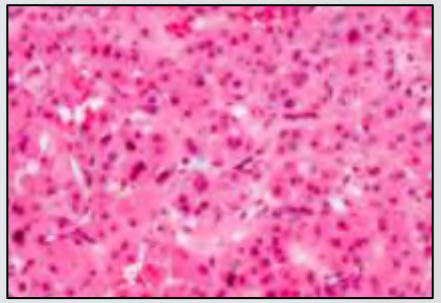


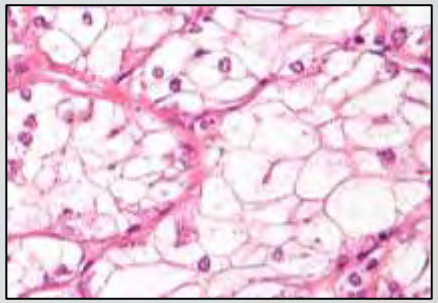
Macklin et al, Eur. Urol. 2019, Kutikov

99^{m}Tc-Sestamibi SPECT/CT

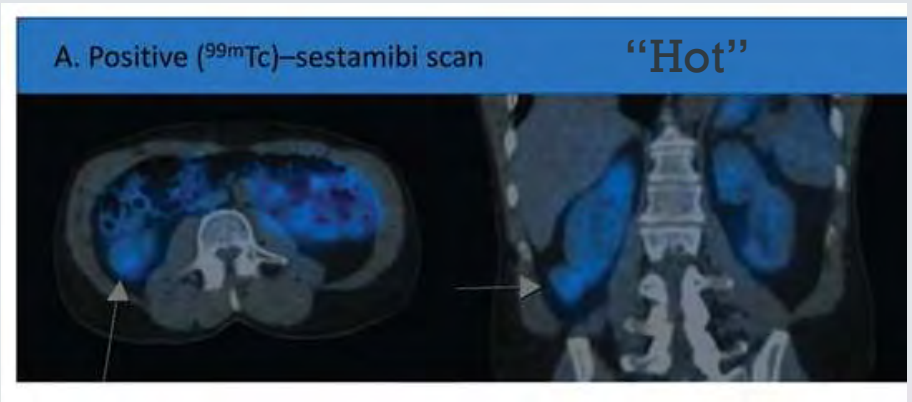


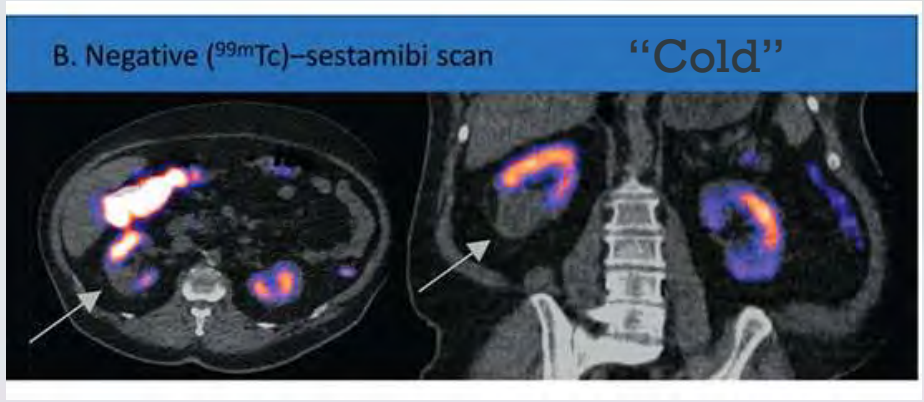






Histology:	Renal parenchyma	Oncocytoma/Chromophobe	Clear cell RCC
Mitochondria density:	⇔Normal	⇧ Dense	⇩ Low
Tracer uptake:	⇔ Reference	⇧ High	⇩ Low

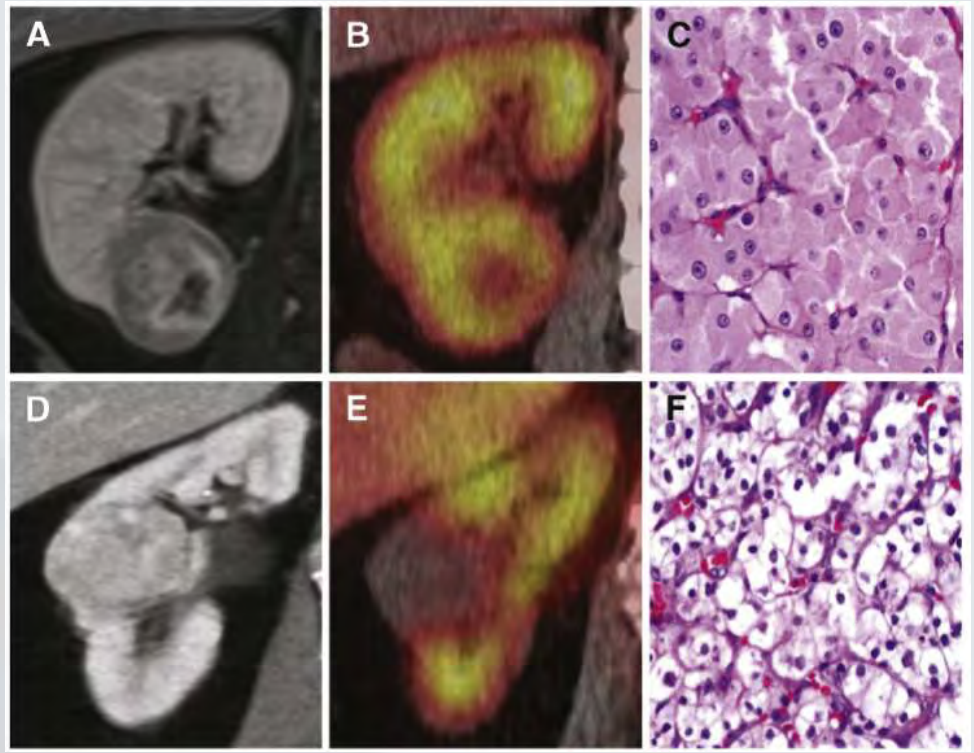


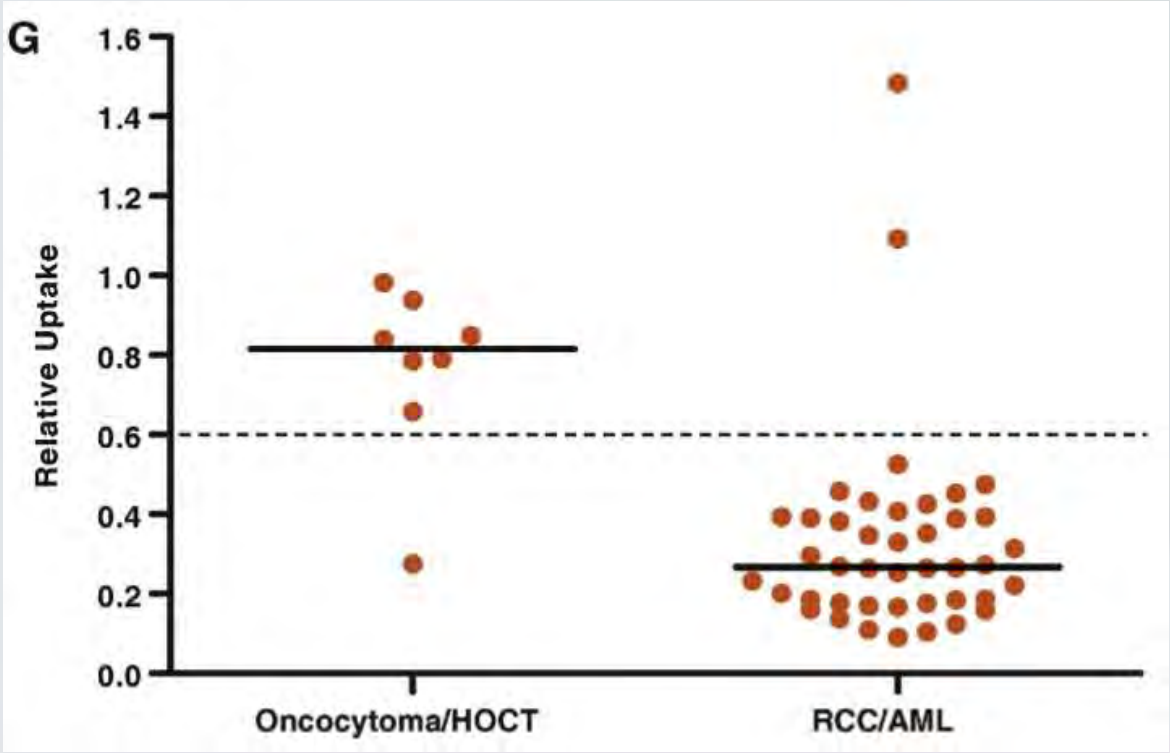


Schober et al, J. Urol. 2023, Gorin et al, Eur. Urol. 2016

Prospective Evaluation of ^{99m}Tc-sestamibi SPECT/CT for the Diagnosis of Renal Oncocytomas and Hybrid Oncocytic/ Chromophobe Tumors

Gorin et al. – 50 patients planned for surgical intervention for cT1 renal mass were imaged with ^{99m}Tc-sestamibi SPECT/CT prior to Sx





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”Positive test” – consistent with oncocytoma

Sensitivity – 87.5%

Specificity – 95.2%

- 2 tumors were “false positives”, but both chromophobe RCC (indolent clinical course)

Histologic type	Central pathology review, *n* (%[a])	Positive on ^{99m}Tc-sestamibi SPECT/CT, *n* (%[b])
Oncocytoma	6 (12)	5 (83.3)
HOCT	2 (4)	2 (100)
Clear cell RCC[c]	26 (52)	0
Papillary RCC[d]	8 (16)	0
Chromophobe RCC	4 (8)	2 (50)
Clear cell papillary RCC	2 (4)	0
Unclassified RCC	1 (2)	0
AML	1 (2)	0
Oncocytoma plus HOCT	8 (16)	7 (87.5)
RCC plus AML	42 (84)	2 (4.8)

^{99m}Tc = technetium-99m; AML = angiomyolipoma; HOCT = hybrid oncocytic/chromophobe tumor; RCC = renal cell carcinoma; SPECT/CT = single-photon emission computed tomography/x-ray computed tomography.

[a] Denominator is the total number of tumors (*n* = 50).

[b] Denominator is the number of tumors of the specified histologic type.

[c] Grade 3–4 tumors: 16 (61.5%).

[d] Grade 3–4 tumors: 4 (50%).

^{99m}Tc-Sestamibi with excellent accuracy

However…

In 7/8 studies results not used in decision-making
➔ all patients proceed with biopsy or surgery

How does this test perform in real-world setting?

Basile et al, Eur. Urol. 2023

Clinical Performance of Technetium-99m–Sestamibi SPECT/CT Imaging in Differentiating Oncocytic Tumors From Renal Cell Carcinoma in Routine Clinical Practice

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[3]Department of Diagnostic Imaging, Fox Chase Cancer Center, Philadelphia, Pennsylvania

Table 2. *Concordance and Discordance Rates for "Hot" and "Cold" Masses That Underwent Intervention With Pathology (Biopsy or Surgery)*

	"Hot" mass	"Cold" mass
All interventions, No./total No.		
Concordant	6/7	36/45
Discordant	1/7	9/45
Surgical pathology, No./total No.		
Concordant	4/4	35/40
Discordant	0/4	5/40
Biopsy pathology, No./total No.		
Concordant	2/3	1/5
Discordant	1/3	4/5

Highlights:

- Integrated 99mTc-Sestamibi SPECT/CT into practice: 71 patients (88 masses)
- Despite "cold" 99mTc-sestamibi imaging, 20% of patients with biopsy or resection had oncocytoma (worse than when we used imaging + biopsy).
- Negative predictive value for absence of oncocytoma in a "cold" mass scan: 80%.

Insights:

- One of the first real-world clinical integrations of 99mTc-sestamibi imaging for small renal masses.
- Provides valuable insights into the utility of this imaging strategy.

Limitations:

- Of the 23 "hot" masses:
  - 7 underwent intervention.
  - Remaining were surveilled.
- Series doesn't provide data on positive predictive value or sensitivity of 99mTc-sestamibi imaging.

Conclusion: 99mTc-Sestamibi SPECT/CT imaging remains investigational.

Schober et al, J. Urol. 2023

Critique

- Reason that assessment varied from current literature was due to qualitative interpretation

Methods:

- Assess performance of ^{99m}TC-Sestamibi SPECT/CT utilizing previously-published quantitative tumor to background ratio (TBR) thresholds compared to when using qualitative (“hot”/“cold”) determinations

- Radiologist review:
  - **“hot”**: mass tracer uptake ≥ renal parenchyma tracer uptake (suggests oncocytoma/HOCT)
  - **“cold”**: mass tracer uptake < renal parenchyma tracer uptake (suggests

- TBRs were calculated by comparing signal counts of the masses to those of the normal ipsilateral renal parenchyma using manually generated regions of interest

- Findings correlated to histology for masses that underwent biopsy or surgical excision

^{99m}TC-Sestamibi Scan Interpretation	Qualitative "hot"/"cold"		TBR ≥ 0.60
Positive (suggest **benign**)* ("hot" or TBR > cutoff)	1 RCC		1 RCC 1 other malignancy
	6 Oncocytoma		10 Oncocytoma
Negative (suggest **malignant**) ("cold" or TBR < cutoff)	34 RCC 2 other malignancy		34 RCC 1 other malignancy
	9 Oncocytoma		5 Oncocytoma
Negative predictive value (rule out oncocytic mass)	**80%**		**88%**
False positive rate (positive scan, malignant tumors)	**1.9%**		**3.8%**

Highest NPV

VS.

* No chromophobe tumors were identified in this series

Limited Utility of Quantitative Thresholds On 99mTc-Sestamibi SPECT/CT For Distinguishing Renal Cell Carcinoma From Oncocytic Renal Masses

Presenter: Alexander Kutikov, MD, FACS

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^{99m}TC-Sestamibi Scan Interpretation	Qualitative "hot"/"cold"	TBR ≥ 0.74
Positive (suggest **benign**)* ("hot" or TBR > cutoff)	1 RCC	0 RCC 1 other malignancy
	6 Oncocytoma	5 Oncocytoma
Negative (suggest **malignant**) ("cold" or TBR < cutoff)	34 RCC 2 other malignancy	35 RCC 1 other malignancy
	9 Oncocytoma	10 Oncocytoma
Negative predictive value (rule out oncocytic mass)	**80%**	**78%**
False positive rate (positive scan, malignant tumors)	**1.9%**	**1.9%**

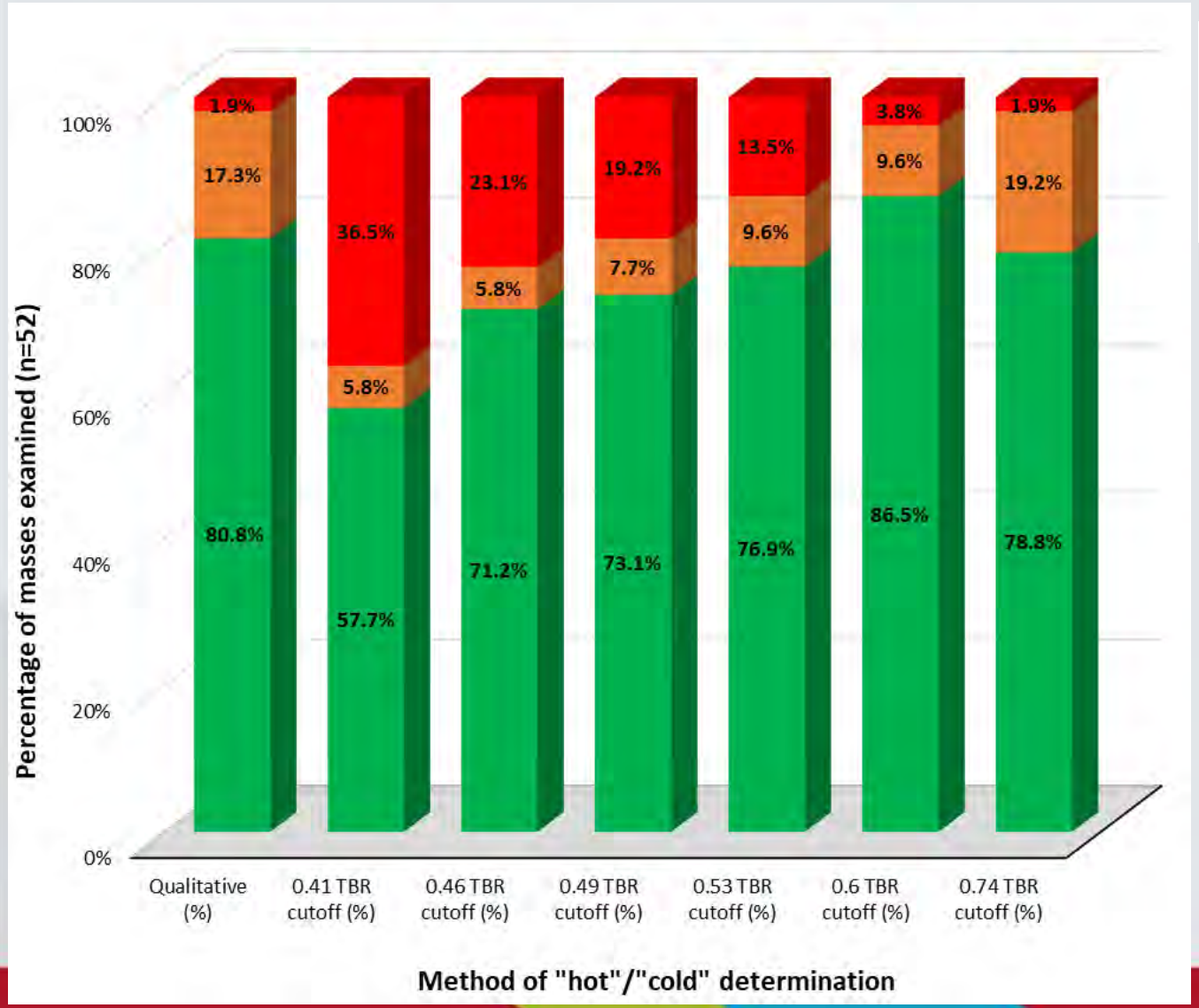
Lowest % False Positive

VS.

* No chromophobe tumors were identified in this series

Limited Utility of Quantitative Thresholds On 99mTc-Sestamibi SPECT/CT For Distinguishing Renal Cell Carcinoma From Oncocytic Renal Masses

Presenter: Alexander Kutikov, MD, FACS



- False positives = "Hot" Malignant Tumors
- False negatives = "Cold" Oncocytomas*
- Concordant = "Hot" Oncocytomas and "Cold" malignant tumors

*** No chromophobe tumors were identified in this series**

Future Directions

Refine:

- Improve accuracy of ^{99m}TC-Sestamibi SPECT/CT in real-world clinical practice

Select:

- Determine best patients for utilization of ^{99m}TC-Sestamibi SPECT/CT imaging

Combine:

- Consider multi-modal approach to diagnosis with cross-sectional imaging, ^{99m}TC-Sestamibi SPECT/CT imaging, and selective biopsy

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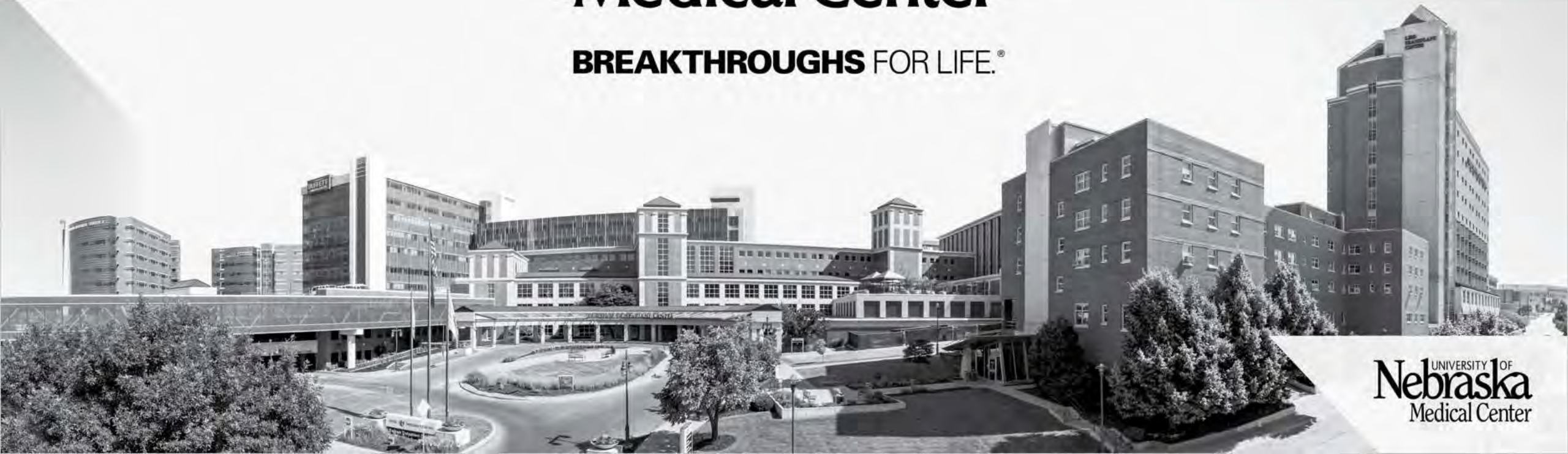

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