NYU Grossman School of Medicine

Radiology Perspective:
Diagnostic Evaluation for MCD Tests

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DISCLOSURES

- Royalties from Wolters Kluwer for unrelated work; honoraria for editorial board work (American Roentgen Ray Society) and educational programming (Radiological Society of North America)
- Grant funding support from the NIH/NIDCR (R01DE030169, S. Kang), NIH/National Cancer Institute (K07CA197134, K07197134-05S1S1, R01CA262375, S. Kang)

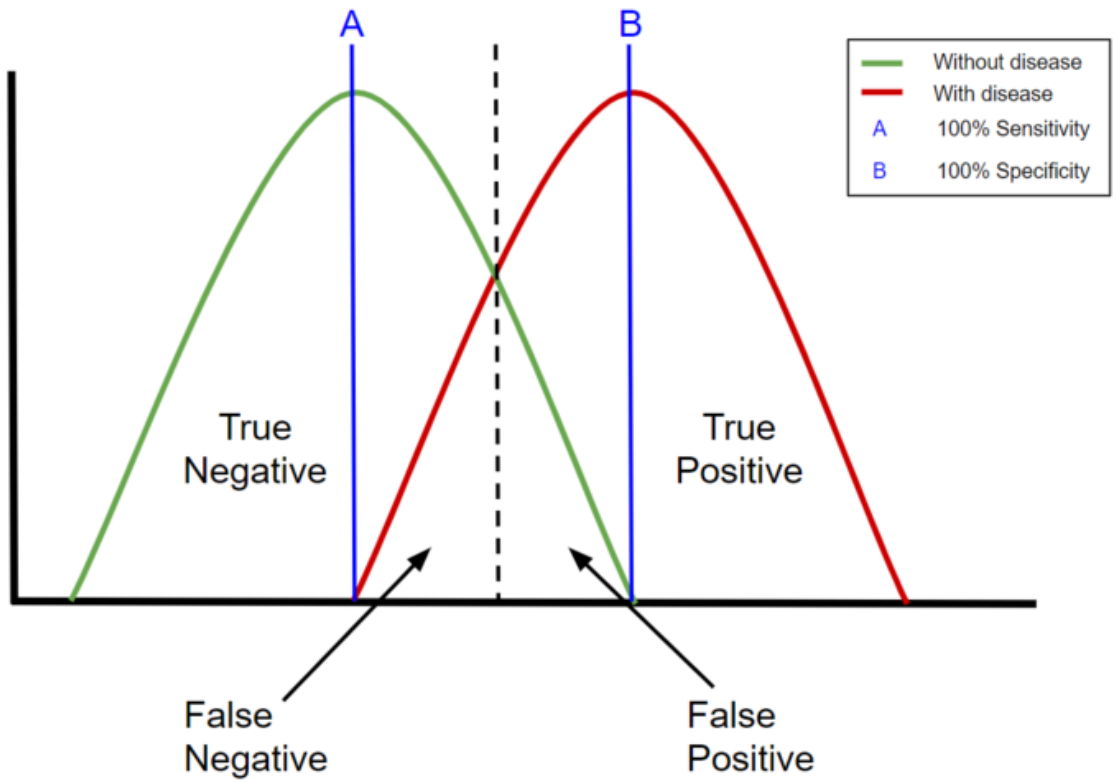
Test	Technology	Organ System or Disease															Size of sample; number with cancer*	Overall sensitivity and specificity (%, 95% CI)	Reported sensitivity for stage I, II cancers respectively (%, 95% CI)
		Bladder	Breast	Colorectal	Esophagus	Head/neck	Kidney	Leukemia	Lymphoma	Liver	Lung	Ovary	Pancreas	Prostate	Stomach	Uterus			
PanSEER (26)	Methylation																828; 414	95.0 (89.0-98.0), 96.1 (92.5-98.3)	N/A
CancerSEEK[a, b] (13, 15)	Mutations, proteins																1,817; 1,005	62 (60-64), 99[c] (N/A)	43 (30-58), 73 (62-84)
Galleri[d] (18)	Methylation																4,077; 2,823	76.3 (74.0-78.5), 99.5 (99.0-99.8)	16.8 (14.5-19.5), 40.4 (36.8-44.1)
DELFI[b] (57)	DNA frag[e]																423; 215	73 (67-79), 98[c] (N/A)	68 (52-82), 72 (62-80)
ThromboSeq[b,f] (58)	RNA Mutation																385; 262	64 (61-66), 99 (95-100)	46 (34-59), 47 (38-57)
MCDBT-1[g] (59)	Methylation																1,050; 505	69.1 (64.8-73.3), 98.9 (97.6-99.7)	35.4 (26.6-45.0), 54.5 (43.6-65.2)
SRFD-Bayes[h] (60)	Methylation																1,700; 1,372	92.1, 99.5[c]	N/A
IvyGene[b,h] (61)	Methylation																197; not reported	84 (75-93), 90 (85-95)	N/A

- **Translation** is the process of turning observations in the laboratory, clinic and community into interventions that improve the health of individuals and the public — from diagnostics and therapeutics to medical procedures and behavioral changes.

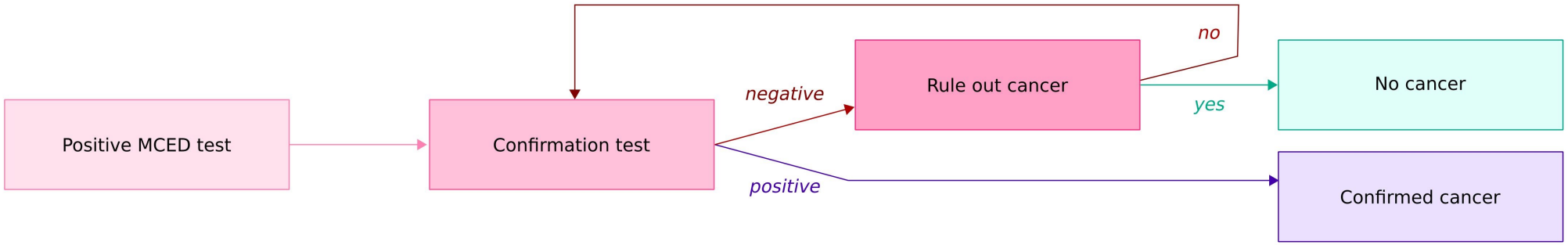
Three Facets for Discussion

- Downstream implications of MCD test performance on diagnostic workup and resolution
- Systems-level access and health system costs for diagnostic evaluation
- The problem of unrelated imaging findings: “the incidentaloma”

Sensitivity vs. Specificity

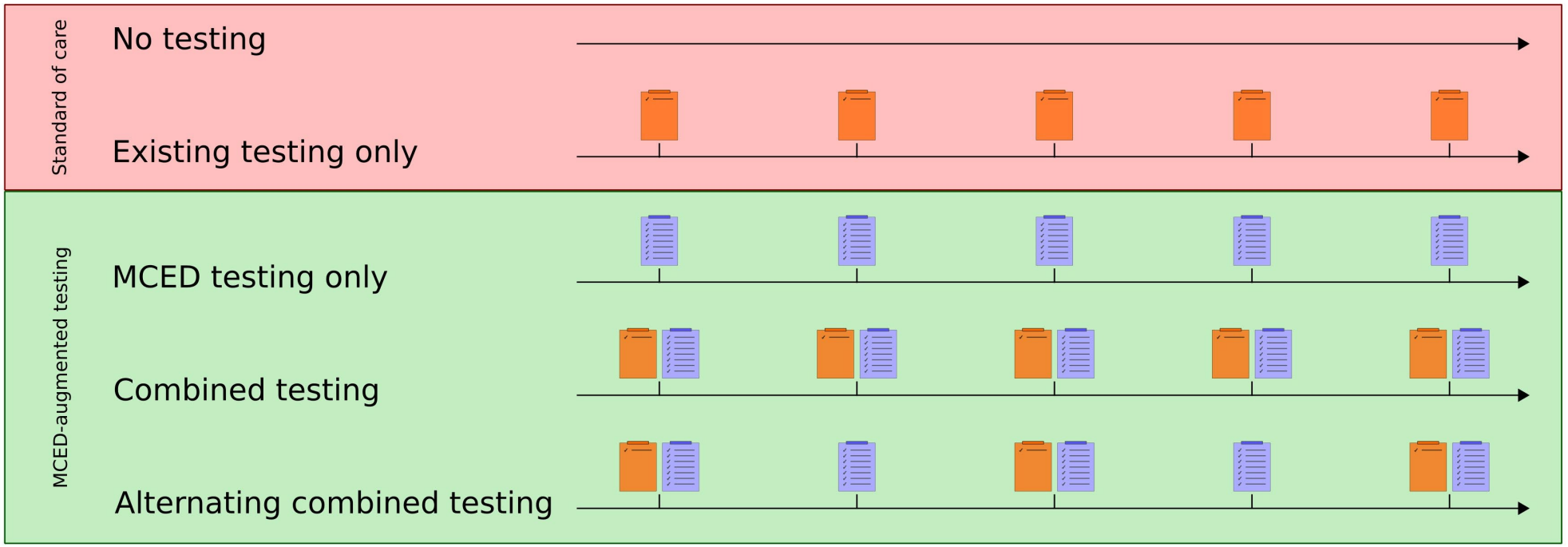


Resolving MCD results given suboptimal performance



Resolve the result: 1) is there a tumor? 2) If it's unclear from the single confirmation test, must be further evaluated.

- Could involve another test (invasive or non-invasive, e.g., endoscopy) or biopsy if there is a visible lesion
- Could also involve monitoring with a repeat imaging test after some time



How should the MCD be evaluated in trials and in practice?

- As a new testing regimen where there is no current screening test
- As a new test if an existing test is suboptimal due to performance, or due to availability or patient acceptability
- As supplemental information
- Will require careful measurement of performance characteristics, time to resolution, and clinical benefits and harms

Problems

- Patients in rural settings, safety net systems may not have easy access to PET scans, PET-CT scans, or MRI.
- Ultrasound and CT have less sensitivity and specificity for some cancers depending on organ system and particularly in early stage

Incidental Findings: Prevalence

Imaging modality	Approximate % cases with IFs
Brain MRI	About 10%
CT Colonography	10-20%
Low Dose Chest CT for lung cancer screening	50%
Chest CT (not lung cancer screening)	19%
Abdomen/pelvis CT	40-70%
Lumbar spine CT	40%

- Some older subpopulations: virtually all patients have IFs
  - About 20% overall may be actionable, needing more diagnostic testing or clinical visits to resolve
  - At least 15% result in consultation with a specialist
- Has led to hesitancy to recommend CT-based cancer screening
- Represent a wide range of risks to patients, with potential for both under- and over-management

Thyroid nodules: >50% prevalence in adults >40 years of age

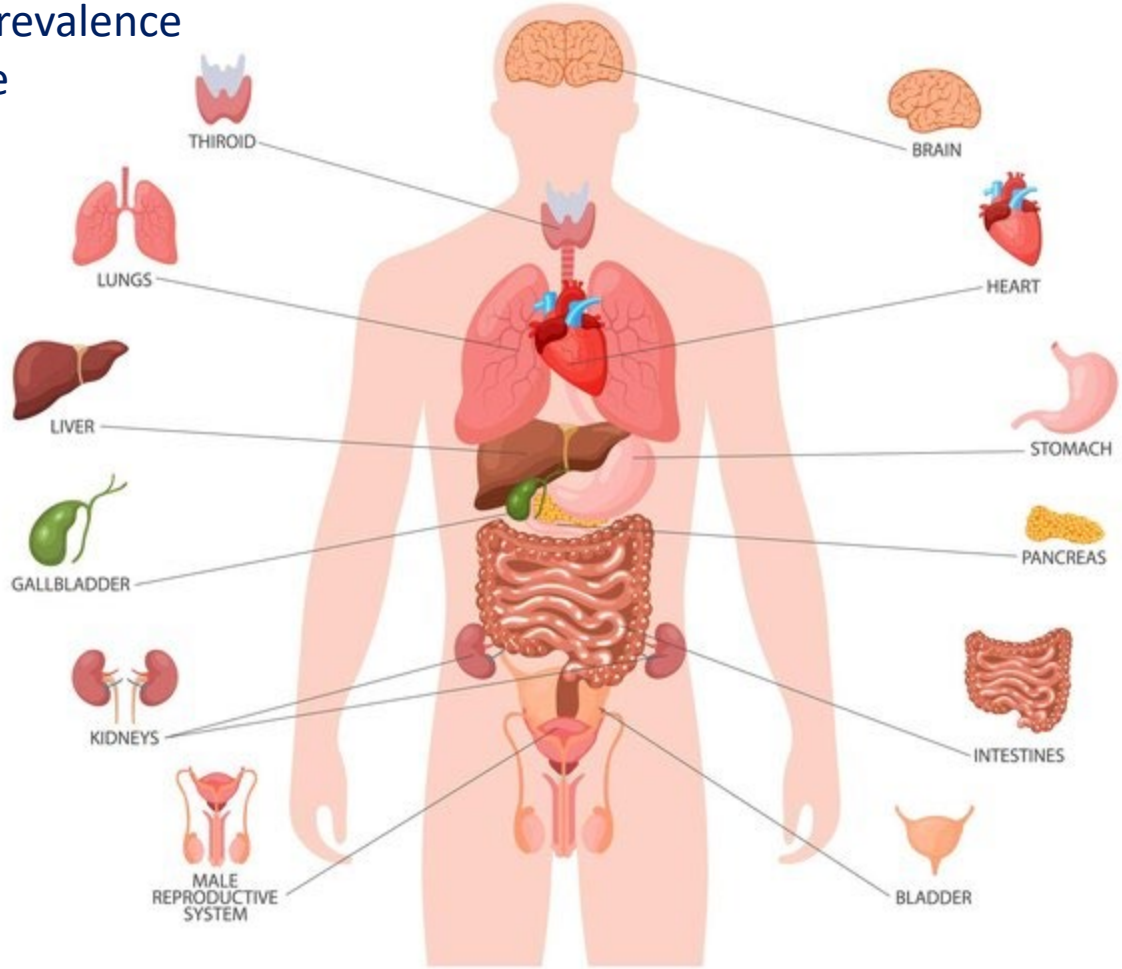
Lung nodules: ~1-1.5 million per year

Solid liver lesions: 6% prevalence

Gallbladder polyps: 4-13% patients

Adrenal nodules: 4-8% prevalence on CT

Kidney cancers: 2-3x incidence from 1970s-2010



… And pancreatic cystic lesions, adnexal lesions, borderline enlarged lymph nodes, small cerebral aneurysms, pineal cysts, pituitary adenomas, bone lesions, etc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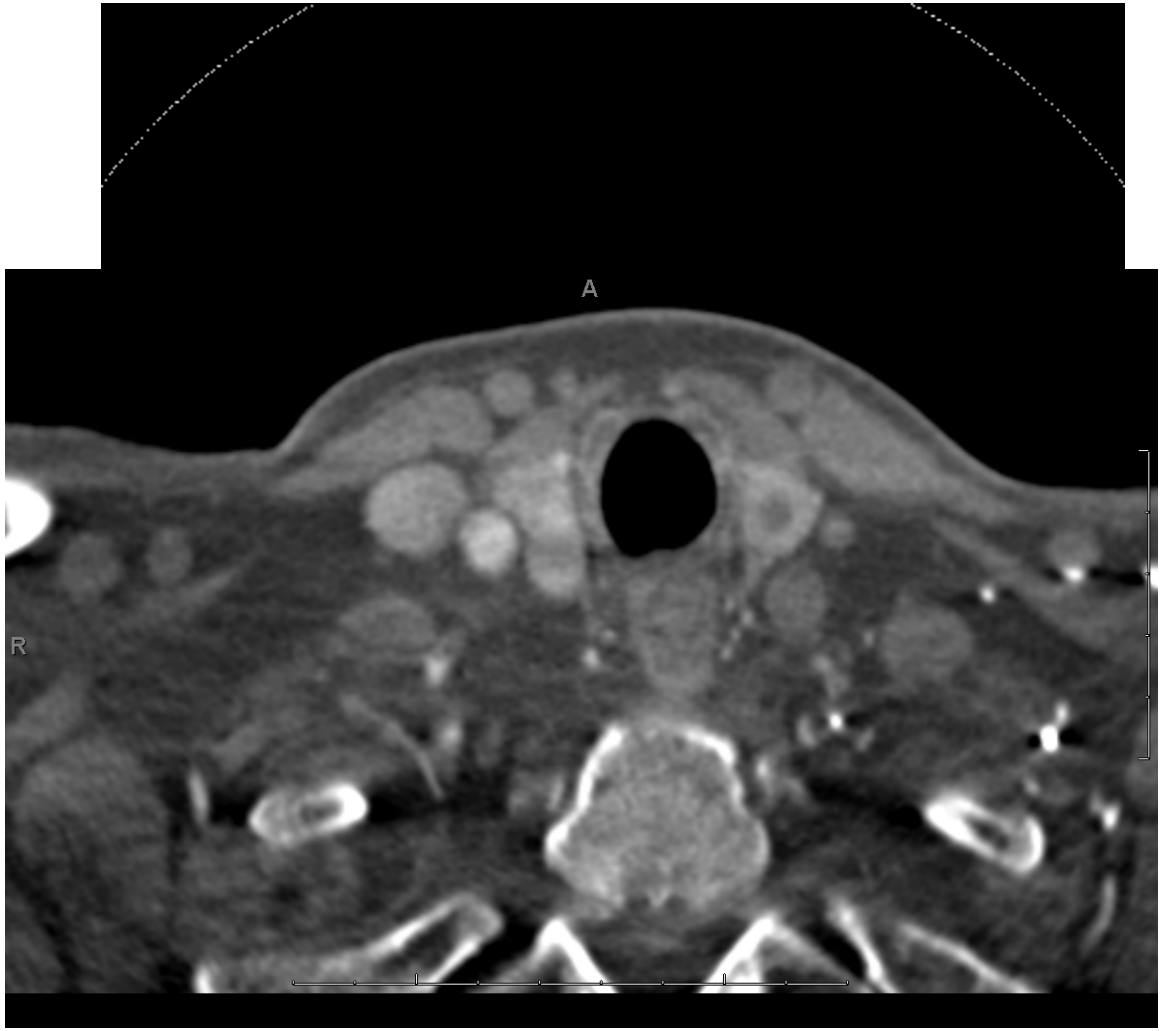
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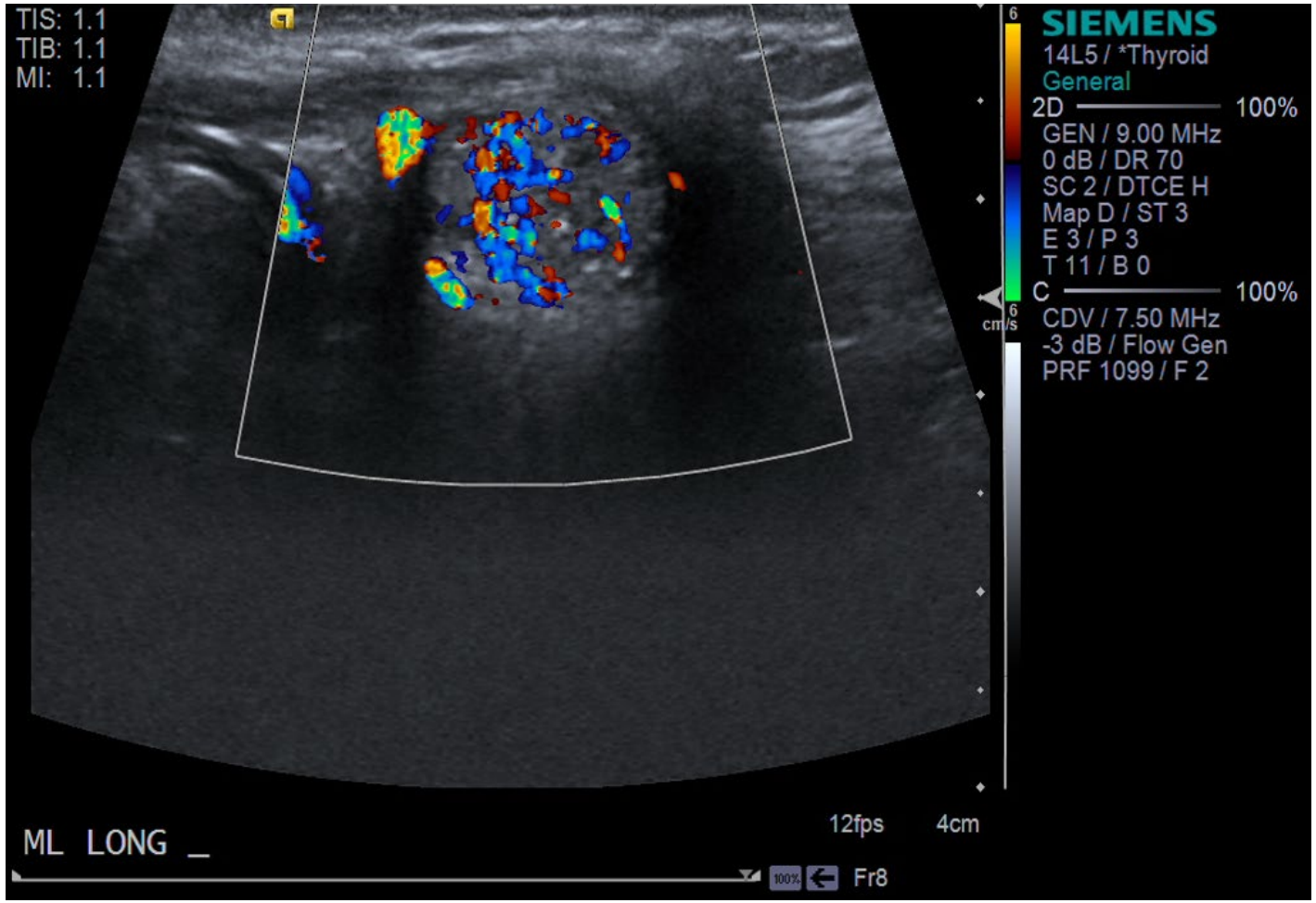

Biopsy proven papillary thyroid carcinoma

Conclusion

- Need careful accounting of diagnostic yield of the MCD itself (separate from the entire diagnostic pathway)
- Separate characterization of imaging findings that are unrelated (incidentalomas)
- Understand downstream costs and potential for bottlenecks for underserved patients
- Impact of implementation should be compared against most relevant comparator technologies and approaches

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