Cost-Effectiveness of an Autoantibody Test as an Aid to Diagnosis of Lung Cancer

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BACKGROUND

- Lung cancer (LC) is commonest cause of cancer death in US, in part because it typically is diagnosed in advanced stages
- Clinical trials suggest screening with computed tomography (CT) may yield favorable shift in LC stage at diagnosis; however, a survival benefit from CT screening has not been convincingly demonstrated
- An autoantibody test (AABT)—EarlyCDT-Lung (Oncimmune Ltd.)—to aid in LC diagnosis has recently been developed:
  - While less sensitive than CT, AABT can detect smaller and less-advanced cancers and has greater specificity
  - Patients positive on AABT—and CT+—are much more likely to have LC and thus may be more aggressively evaluated and treated

STUDY OBJECTIVE

- To estimate cost-effectiveness of using AABT as an aid to CT in the detection of LC in high-risk patients

STUDY METHODS

Model Description

- Model depicts clinical and economic consequences of alternative strategies for LC screening in cohort of 100,000 previously unscreened high-risk patients
- Model considers a single "prevalence-round" screening exam
- Screening strategies include:
  - CT followed by AABT if positive (CT→AABT)
  - CT alone
  - No Screening
- Patients assumed to be at high-risk of having previously undetected LC—NSCLC or SCLC—due to current or former smoking—and to be 60 years of age:
  - NSCLC stratified based on nature of disease—aggressive vs indolent; all SCLC assumed to be aggressive
- Patients classified into one of four groups—true-positive, true-negative, false-positive, or false-negative—based on LC+ and screening+ vs screening-
- True-positives undergo further diagnostic evaluation followed by LC treatment:
  - Diagnostic tests employed, and their scheduling, depend on whether CT and AABT are positive or just CT, and nodule size
  - Detection of aggressive NSCLC and SCLC by screening confers advantages in terms of earlier stage at diagnosis and smaller tumor size (NSCLC stage 1 only), both of which offer survival benefits
  - Patients with CT+ and AABT+ receive more aggressive evaluations—vs those with CT+ only—which results in stage, size, and survival benefits
  - Detection of indolent NSCLC by screening ("overdiagnosis bias") generates additional costs but confers no survival benefit

Model Description (Cont.)

- True-negatives undergo no further diagnostic evaluation
- False-positives undergo additional evaluation that ultimately rules out diagnosis
- False-negatives with aggressive NSCLC or SCLC are correctly diagnosed—on average—12 months following screening and subsequently undergo LC treatment:
  - Cancer assumed to be more advanced than that for true-positives
  - Most patients with false-negative indolent NSCLC are never diagnosed
- Costs include: initial screening (all patients); follow-up diagnostic evaluation (true-positives and false-positives); LC treatment (true-positives and false-negatives)
- Study perspective was that of a healthcare system
- Future benefits and costs (2008US$) discounted at 3% per year

Model Estimation

- LC prevalence estimated assuming a three-year "look-forward period":
  - AABT+ could result from tumor detectable by CT at that time or from one so small it would not be detectable by CT for up to three years
- CT sensitivity/specificity calculated from "prevalence-screen" perspective based on results of Mayo Clinic study[1-3]; for AABT, estimates based on published data[4,5]

Table 1. Estimated values of selected model parameters

Model Parameter	NSCLC	SCLC	Reference
Disease Characteristics			
Prevalence of Lung Cancer, %	3.20%	0.56%	1-3, 6, 7
Type of Lung Cancer, %	85%	15%	7
Screening Test Characteristics			
CT			1-3
Sensitivity	47%	47%	
Specificity	49%	49%	
AABT			4, 5
Sensitivity	40%	40%	
Specificity	90%	90%	
Stage Shift vs No Screening, %			
CT	50%	25%	8 (NSCLC), Expert Opinion (SCLC)
AABT	80%	40%	Expert Opinion
CT→AABT	62%	31%	Derived
Size Shift (Stage 1) vs No Screening, mm			
CT	16.0	---	2
AABT	18.0	---	Expert Opinion
CT→AABT	16.8	---	Derived
Overdiagnosis Bias, %	27%	---	9
Costs			
Initial Screen			
CT	$301	$301	10
AABT	$300	$300	Assumed
LC Treatment			11
Initial Year (Stage 1 - 4)	$35,871 - $50,346	$50,346	
Continuing Years (Annual)	$4,576	$4,576	
Last Year of Life (Stage 1 - 4)	$46,295 - $78,623	$78,623	

Analyses

- Cost-effectiveness calculated as ratio of difference in expected costs to differences in expected life-years (LYs) and expected quality-adjusted life-years (QALYs) between:
  - CT→AABT vs No Screening
  - CT→AABT vs CT alone
  - CT vs No Screening

RESULTS

Outcomes

- Of 2,901 LC cases, 1,363 (true-positives) would be detected with CT→AABT or CT alone; screening would yield 49,079 false positives

Table 2. Classification of patients from screening for lung cancer with CT and CT → AABT, respectively, in a hypothetical population of 100,000 current/former smokers

	No Screening	CT	CT → AABT	CT → AABT vs No Screening	CT → AABT vs CT	CT vs No Screening
True Negatives	96,234	47,155	47,155	-49,079	0	-49,079
False Positives	---	49,079	49,079	49,079	0	49,079
True Positives	---	1,770	1,770	1,770	0	1,770
NSCLC	---	1,505	1,505	1,505	0	1,505
Aggressive	---	1,098	1,098	1,098	0	1,098
Indolent	---	407	407	407	0	407
SCLC	---	265	265	265	0	265
False Negatives	3,766	1,996	1,996	-1,770	0	-1,770
NSCLC	3,202	1,697	1,697	-1,505	0	-1,505
Aggressive	2,337	1,239	1,239	-1,098	0	-1,098
Indolent	865	458	458	-407	0	-407
Detected	123	0	0	-123	0	-123
Undetected	742	458	458	-284	0	-284
SCLC	564	299	299	-265	0	-265

- Screening with CT→AABT or CT alone would increase (discounted) costs of care by $965 and $802 per patient, respectively, and yield an additional 0.048 and 0.040 LY per patient and 0.032 and 0.026 QALY per patient, respectively, vs no screening
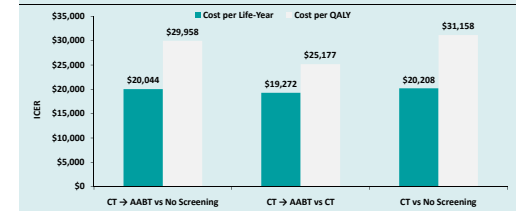
Table 3. Outcomes from screening for lung cancer with CT and CT → AABT, respectively, in a hypothetical population of 100,000 current/former smokers*

	No Screening	CT	CT → AABT	CT → AABT vs No Screening	CT → AABT vs CT	CT vs No Screening
Life-Years	1,505,557	1,509,526	1,510,371	4,814	845	3,969
Quality-Adjusted Life-Years	1,303,417	1,305,991	1,306,638	3,221	647	2,574
Cost	$230,946,859	$311,161,933	$327,436,131	$96,489,272	$16,274,198	$80,215,074
Screening	$0	$30,051,000	$43,780,230	$43,780,230	$13,729,230	$30,051,000
Diagnostic Follow-up	$10,480,549	$51,227,441	$55,250,510	$44,769,961	$4,023,069	$40,746,892
Treatment	$220,466,310	$229,883,492	$228,405,391	$7,939,081	-$1,478,101	$9,417,182

*Discounted value

RESULTS (CONT.)

Cost-Effectiveness


Figure 1. Cost-effectiveness of screening for lung cancer with CT → AABT vs No Screening and CT, respectively, and CT vs No Screening

- Cost per Life-Year: CT → AABT vs No Screening $20,044; CT → AABT vs CT $19,272; CT vs No Screening $20,208
- Cost per QALY: CT → AABT vs No Screening $29,958; CT → AABT vs CT $25,177; CT vs No Screening $31,158

Sensitivity Analyses

- Cost-effectiveness highly sensitive to assumed stage shift, and moderately sensitive to cost of AABT and prevalence of undiagnosed LC

Figure 2. Cost-effectiveness of CT → AABT vs CT, by absolute difference in NSCLC stage shift
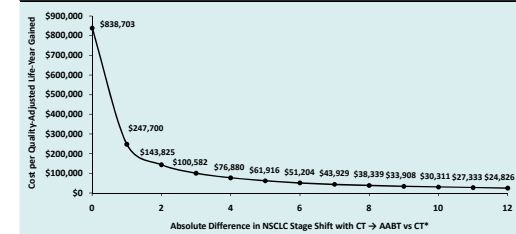
*NSCLC stage shift varied between 50% and 62% for CT → AABT strategy and held constant at 50% for CT strategy. SCLC stage shift held constant at 25% for both strategies.

CONCLUSION

- Under our base case assumptions, and reasonable variations thereof, using AABT—EarlyCDT-Lung—as an aid to CT in screening high-risk patients for LC is cost-effective in comparison with no screening or screening with CT alone

REFERENCES

1. Swensen, Am J Respir Crit Care Med 2002; 165:508-13
2. Swensen, Radiology 2003; 226:756-61
3. Swensen, Radiology 2005; 235:259-65
4. Spitz, J Natl Cancer Inst 2007; 99:715-26
5. SEER Cancer Statistics Review 1975-2006, NCI website 2009
6. Mahadevia, JAMA 2003; 289:313-22
7. Boyle, JCO 2010; in press
8. Murray, Ann Oncol 2010; doi:10.1093/annonc/mdp606
9. Lindell, Radiology 2007; 242:555-62
10. RBRVS 2008; Chicago, Ill: American Medical Association
11. Yabroff, J Natl Cancer Inst 2009; 101:1161-63