The impact of Percepta Genomic Sequencing Classifier (GSC) on clinical decision making in patients with a high- risk lung nodule

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Background

- Current guidelines recommend that patients who have lung nodules with a high probability of malignancy (>65%) and no evidence of metastatic disease should undergo either surgical resection or other ablative therapies.[1]
- However, prior studies have shown that physicians may opt for more conservative management including further surveillance or other diagnostic procedures in these high-risk patients.[2,3]
- Percepta Genomic Sequencing Classifier (GSC), a classifier developed using whole transcriptome sequencing from bronchial epithelial cells and clinical factors to assess risk of lung cancer in lung nodules, was designed to risk stratify lung nodules by down classifying risk of malignancy (ROM) as a “rule -out“ test with high sensitivity as well as up-classifying ROM as a “rule- in” test with high specificity for malignancy.[4,5]

Objective and Hypothesis

- The primary objective of this study was to determine the impact of a Percepta GSC up-classification from pre-test high-risk (>60%) to post-test very high-risk (>91%) in the initial management of lung nodules.

- We hypothesized that up-classification by Percepta GSC from pre-test high-risk to very high-risk will result in an earlier decision to recommend either surgical resection or other ablative therapy and avoid additional procedures as recommended by the American College of Chest Physician (ACCP) guidelines.[1]

Methods

- This prospective randomized decision impact survey included 37 patient cases with an indeterminate lung nodule from the AEGIS I/ II cohorts and the Percepta Registry who:
  - were undergoing work up of a lung nodule and had a non-diagnostic bronchoscopy
  - had a nodule that had high pre-test ROM (>60%) that was up-classified to very high ROM (> 91%) by Percepta GSC.
- 97 US- based Licensed Pulmonologists were selected to take this survey that included 10 randomly assigned patient cases from the 37 cases.
- The physician survey takers were presented each patient case and then asked about their recommended management plan which may have included a diagnostic or surveillance procedure, surgical resection or other ablative therapy.
- For each case, physician survey takers were first presented with the patient's clinical information without Percepta GSC and then with Percepta GSC.
- 97 survey takers provided a total of 682 evaluations of the 37 patients (341 cases evaluations prior to and after Percepta GSC results).

Results- Table 1. Demographics of Survey Takers

Survey Taker Characteristics	N=97[1]
Use of Percepta in medical practice	
Yes	53 (55%)
No	44 (45%)
Medical Specialty	
Interventional Pulmonology	27 (28%)
Pulmonary Critical Care	27 (28%)
Pulmonology	43 (44%)
Length of time in medical practice (years)	13 (8,23)
Region of medical practice (within the US)	
Midwest	27 (28%)
Northeast	27 (28%)
South	29 (30%)
West	14 (14%)
Medical practice setting	
Academic or Teaching Hospital	46 (47%)
Community-Based	51 (53%)
Bronchoscopies performed for suspect lung cancer (monthly)	15 (10, 25)

[1]n (%); Median (IQR, interquartile range)

Results-Table 2a. Demographics of the Patient Survey Cases

Patient Characteristics		N=37
Cohort	AEGIS I/ II	30 (81%)
	Percepta Registry	7 (19%)
Age	Years (Median (IQR))	73 (69,77)
Race	White	28 (76%)
	Black	7 (19%)
	Other	2 (5%)
Sex	Female	17 (46%)
	Male	20 (54%)
Smoking Status	Current smoker	19 (51%)
	Former smoker	18 (49%)
Tobacco pack years	Years (Median (IQR))	59 (40,82)

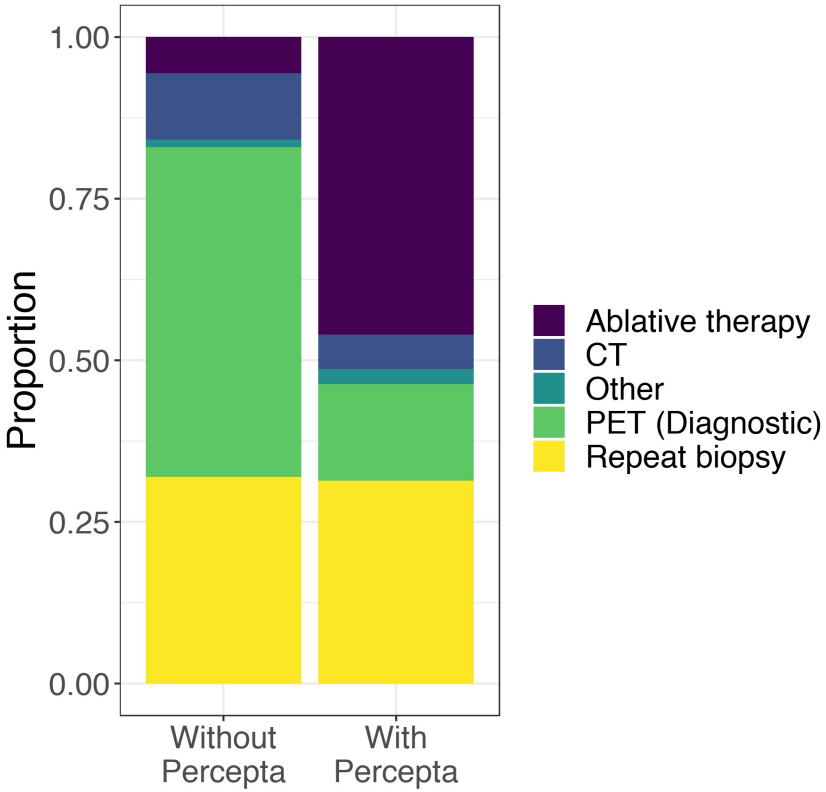
IQR= Inter-quartile range

Results-Table 2b. Nodule Characteristics of the Patient Survey Cases

Nodule Characteristics		N=37
Nodule size (mm)	Median (IQR)	20 (16,28)
Nodule Location	Central	7 (19%)
	Peripheral	23 (62%)
	Both	7 (19%)
Lung Cancer (Histologic type)	Non-small-cell	30 (81%)
	Adenocarcinoma	13 (35%)
	Squamous	8 (22%)
	Not specified/Unknown	9 (24%)
	Small-cell (Limited stage)	2 (5%)
	Unknown	3 (8%)
Benign		2 (5%)

Mm, millimeters; IQR, Inter-quartile range

Results- Percepta GSC very high ROM (>91%) result significantly increases the number of surgical resection/ablative therapies in lung nodules

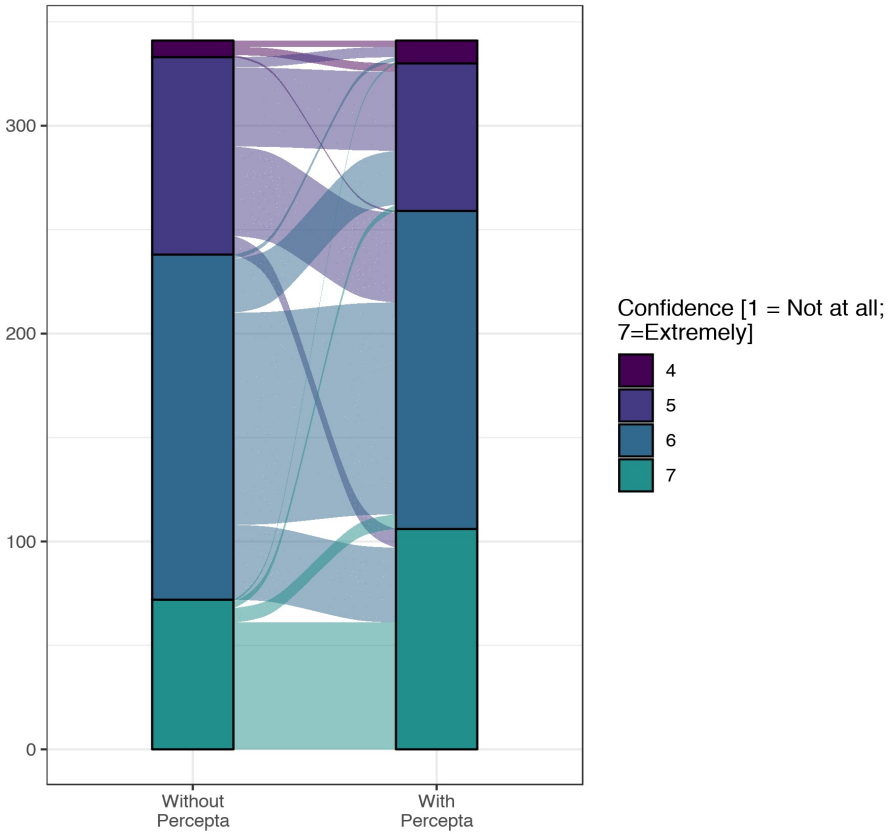


Recommended next step in patient cases	Without Percepta GSC	With Percepta GSC very high ROM result*
Ablative Therapy (Surgical Resection or SBRT)	19 (5.6%)	157 (46%)
Chest CT scan	35 (10%)	18 (5.3%)
Other	4 (1.2%)	8 (2.3%)
PET scan (diagnostic)	174 (51%)	51 (15%)
Repeat Biopsy**	109 (32%)	107 (31%)

*Odds ratio of 4.76, p-value < 0.001

** Includes Bronchoscopic biopsy or Transthoracic needle biopsy/aspirate (TTNB/TTNA)

Results- Percepta GSC very high ROM (>91%) result increases confidence in recommended management of lung nodules



- Percepta GSC increased the number of extremely confident recommendations from 72/341 (21%) to 106/341 (31%) evaluations.
- Overall, more physicians had an increased level of confidence with Percepta GSC [93 versus 44] (p value = 0.002).

Scale from questionnaire:

22. How confident are you in recommending this as the next step? (Select one)

Not at all Confident			Neutral			Extremely Confident
1	2	3	4	5	6	7

Conclusions

- Percepta GSC had a quantifiable impact on clinical decision making in patients with a pre-test high risk lung nodule that was up-classified to very high-risk (>91%) for malignancy.
- The very high-risk classification by Percepta GSC significantly increased the recommendation for surgical resection/ ablative therapies and the confidence of this next management step in accordance with the ACCP guideline recommendations.
- By up-classifying nodules from high to very high ROM, Percepta GSC will improve the likelihood and timeliness of appropriate therapies and enable physicians to more effectively manage patients to improve patient outcomes.

References

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