AN AI-BASED QUALITY CONTROL SYSTEM IN A CLINICAL WORKFLOW SETTING

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ABSTRACT

Introduction

- Maccabi Healthcare Services is a large healthcare provider with a centralized pathology institute, handling 120,000 histology accessions per year, of which 700 are prostate core needle biopsies (PCNBs).
- While cases that are diagnosed as cancerous undergo independent review by a second pathologist, 60% of PCNBs are diagnosed as benign by a single pathologist and do not undergo further review.
- Ibex Medical Analytics has developsed a software that, through the identification of various cell types and features within whole slide images of PCNBs, alerts pathologists in cases of discrepancy between their diagnosis and the Ibex Second Read™ (SR) system's algorithm for prostate.

Methods

- Two studies were conducted: (1) A retrospective study, in which the algorithm was run on 80 cases previously diagnosed by a pathologist as benign, as well as on samples from two additional institutes. (2) A prospective study in which the algorithm was deployed as a QC system on all new PCNBs, beginning March 2018.
- In both studies the system raised alerts when encountering discrepancies between the automated analysis and the pathologist's diagnosis, prompting a second pathologist review.
- The performance of the algorithm, including AUC, sensitivity and specificity, were assessed, as compared to a gold-standard of the pathologist's diagnosis.

Results

- Retrospectively, the algorithm identified missed cancers in all three institutes. In Maccabi, two cases of missed cancer were identified by the algorithm. In both cases, the algorithm identified small foci of Gleason 3, subsequently confirmed by IHC. EMR data for these cases demonstrated that 2 years after the initial biopsy, the patients were diagnosed with higher grade cancer and underwent radical prostatectomies. Cases of missed cancers identified in the two additional institutes were confirmed by a second pathologist review as cancerous.
- The algorithm's performance on the retrospective data from the three institutes is detailed in Table 1 in the results section.
- Prospectively, deployment of the algorithm in Maccabi identified a case of low-grade cancer diagnosed by the pathologist as benign.

Conclusions

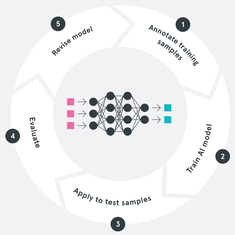
AI-based diagnosis in prostate cancer can increase diagnostic speed and accuracy, and has demonstrated clinical utility. To our knowledge, this is the first AI-based digital pathology diagnostic system running in a live clinical setting.

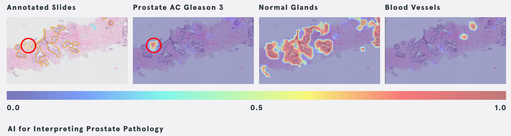
IBEX

BACKGROUND

ALGORITHM DEVELOPMENT

- Philips Intellisite® scanner
- 6,000 retrospective cases scanned to date (70,000 slides)
- Slide sets from 4 additional institutes
- All new prostate biopsies are scanned routinely
- A fraction of the slides is annotated in detail by senior pathologists
- Built system based on deep-learning models trained on annotated slides





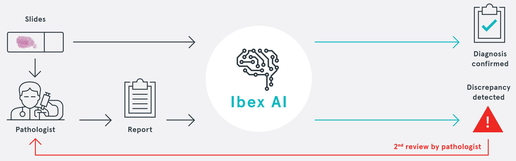
METHODS

Retrospective validation

- Data from three independent institutes
- All slides diagnosed by a pathologist as benign in a defined time period to avoid bias in slide selection

Prospective quality control

- Algorithm is deployed as QC system on all new PCNBs in Maccabi, beginning March 2018
- The system raises alerts in case of discrepancy between automated analysis and pathologist diagnosis
- The alert prompts review by a pathologist to resolve the discrepancy



RESULTS

ALGORITHM PERFORMANCE

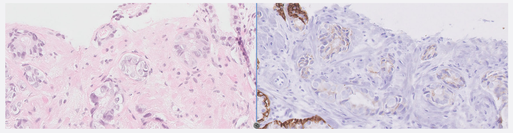
Prostate Cancer Detection Algorithm Results

	Maccabi	Institute #2	Institute #3
AUC	0.97	0.99	0.99
Sensitivity	96%	99%	99%
Specificity	90%	90%	90%
Validation (# slides)	1333	728	283
Missed Cancers Identified	**2/80**	**1/26**	**1/30**

Table 1: Performance of the prostate cancer detection algorithm on three institutes. All validation data is independent of training data. AUC: area under the curve.

CANCERS MISSED

AI detected cancer in **4 out of 136** randomly selected retrospective cases originally diagnosed as benign.



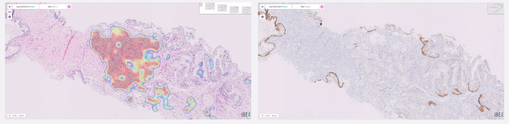
- Left-hand-side of figure: Site of one of the areas marked as suspicious by the Ibex SR system
- Right-hand-side of figure: The respective site in the CK903 slide shows no expression, confirming it as malignant

MISDIAGNOSIS DETECTED

- 55 year old male
- Pathologist diagnosis: Benign
- **Ibex SR: Cancer Alert, 99.3% confidence**

Diagnosis revised to AC G3+3

Impact on treatment



Portion of H&E image with algorithm results (red = high probability for cancer)

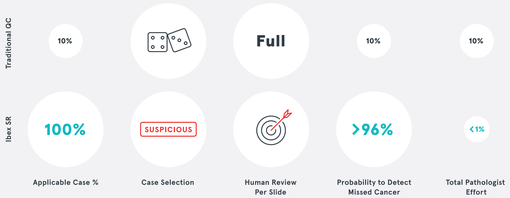
Portion of confirmatory IHC (ck903) image (unstained glands positive for adenocarcinoma)

DISCUSSION

- In the retrospective data, the Ibex SR system achieved high AUC value
- A specificity of 90% was selected arbitrarily, representing a 10% false-positive rate, as well as the QC sampling rate defined by the lab
- At 90% specificity, sensitivity values for the three sites were 0.96, 0.99 and 0.99, representing the probability to detect a malignancy in cases diagnosed incorrectly by a pathologist as benign
- The Ibex SR system's false-negative rate, i.e. the probability missing a malignancy in cases diagnosed incorrectly as benign (equal to [1-sensitivity]), was 0.04 for Maccabi, and 0.01 for the two other institutes

SUMMARY AND CONCLUSIONS

- The Ibex SR system is the first AI-based diagnostic system to be deployed in routine clinical setting in a pathology lab
- The system enables a second read on 100% of the cases, in parallel to pathologist diagnosis, to enable cost-effective, rapid and accurate diagnosis
- Proven clinical utility in identifying both retrospective and prospective misdiagnoses



ACKNOWLEDGEMENTS

- Morris Kahn Maccabi Health Data Science Institute

MKT00002 Rev. A