Deployment of a multi-tissue AI-based quality control system in routine clinical workflow

Judith Sandbank[1,2], Ira Krasnitsky[1], Issar Yazbin[1], Inbal Gross[1], Ronen Heled[1], Arthur Rozenberg[1,2], Ronen Cypis[1], Rachel Mikulinsky[1], Einav Shnaidman[1,2], Geraldine Sebag[1]

1 Ibex Medical Analytics Ltd., Tel Aviv, Israel 2 Maccabi Healthcare Services, Israel

Contact: Judith.Sandbank@ibex-ai.com

BACKGROUND

- Maccabi Healthcare Services, a large healthcare provider with a centralized pathology institute, receives samples from 350 clinics & hospitals and handles 140,000 accessions/year
- A significant portion of the histopathology cases are prostate core needle biopsies ~700 cases/year (>8,000 slides) and breast biopsies ~7000 cases/year (>35,000 slides)
- Maccabi is staffed with 11.5 FTE pathologists ,~20K cases/year per pathologist
  - The very heavy case load leads to potential errors and significant delays in reporting, as well as inability to implement QC
- AI-based solutions that support pathologists in their diagnostic work have the potential to relieve this burden
- Ibex Medical Analytics develops AI-based diagnostic solutions for pathology, including Galen™ Prostate CE-IVD marked solution, which detects and grades prostate core needle biopsies, and Galen™ Breast solution, which detects invasive and in-situ carcinomas in breast biopsies

OBJECTIVE

To assess the clinical utility of Galen Prostate and Galen Breast solutions deployed as a QC system on all new prostate and breast biopsies entering the lab in routine clinical use at Maccabi

METHODS

- Slides are scanned using a Philips IntelliSite Scanner at 40x magnification (pixel resolution of 0.25 µm/pixel).
- The underlying algorithms utilize state-of-the-art Artificial Intelligence (AI) and Machine Learning techniques, and were trained on >2M image samples, obtained from slides from multiple labs and geographies, and manually annotated by senior pathologists.
- The prostate algorithm was validated with outstanding results in a recently publised study and conducted at UPMC (Pantanowitz et al. 2020). The validation of the breast algorithm is shown here (see Table 2)
- The Second Read system runs in parallel to the pathologists' routine workflow and raises alerts when encountering discrepancies between the automated analysis and the original pathologist's diagnosis, prompting a second pathologist review (see Figure 1).
- Galen Prostate solution raises two types of alerts:
  a) Slides from benign cases that have a high suspicion of cancer
  b) Slides from G3+3 cancer cases that have a high suspicion of G7+
- Galen Breast solution raises the following alerts:
  a) Invasive cancer alert on slides from benign and DCIS/ADH cases that have a high suspicion of invasive cancer (both IDC and ILC)
  b) Ductal carcinoma in situ (DCIS) alert that also includes Atypical ductal hyperplasia (ADH) on slides from benign cases that have a high suspicion of DCIS/ADH

RESULTS

COMPUTATIONAL AND CLINICAL WORKFLOW OF GALEN SECOND READ SOLUTION

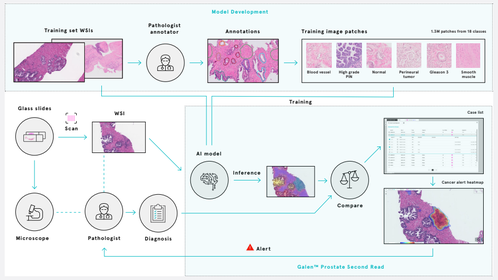


Figure 1. Overview of the algorithm development and clinical deployment of the Galen Prostate solution. The breast algorithm was trained and deployed in a similar way.

From 0% to 100% QC using AI

GALEN PROSTATE DEPLOYMENT STATISTICS

Deployment (03/2018-09/2020)	Total	Benign (%)	Adenocarcinoma (%)	Gleason 3+3/ ASAP	Gleason 7+
# Cases	1,032	465 (45%)	567 (55%)	287	280
# H&E Slides	12,620	5,739	6,861	3,682	3,199

Table 1. Pathologists' diagnoses for the cases analyzed by the Galen Prostate

- **Cancer alerts** were raised for 583 (10.1%) slides from 232 cases diagnosed by pathologists as benign
- **Gleason 7+ alerts** were raised for 93 (5.3%) slides from 137 cases diagnosed as Gleason grade 3+3 (alert deployed from Feb 2019)
- Alerts were focused on specific areas and visualized with associated heatmaps. Therefore, review time was minimal, resulting overall in ~1% of pathologist FTE

GALEN BREAST RETROSPECTIVE VALIDATION

Dataset: **1,129** cases (with 2,360 H&E slides); consecutive cases from 11-12/2018

The table below shows very high performance of the breast algorithm on invasive and in situ cancer detection

Test	# of cases	AUC	Specificity	Sensitivity
Invasive	178 invasive 951 w/o invasive	0.998	97.6%	98.9%
DCIS	40 DCIS 911 w/o DCIS or invasive	0.994	96.5%	97.5%

Table 2. Breast algorithm performance

GALEN BREAST DEPLOYMENT STATISTICS

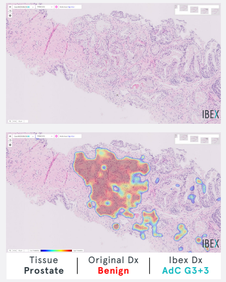
Deployment (12/2019-09/2020)	Total	Benign (%)	Invasive (%)	DCIS (%)	Invasive & DCIS (%)
# Cases	3,878	2,929 (76%)	710 (18%)	143 (4%)	96 (2%)
# H&E Slides	7,584	5,818	1,121	472	173

Table 3. Pathologists' diagnoses for the cases analyzed by the Galen Breast

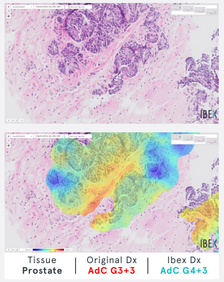
- **Invasive cancer alerts** were raised for 291 (5%) benign slides from 219 cases and for 84 (17.8%) slides from 143 cases diagnosed with DCIS
- **DCIS alerts** were raised for 249 (4.3%) slides from 172 cases diagnosed as benign
- Misdiagnoses were identified and revised during the clinical deployment (see examples) - full details are not disclosed
- Alerts were focused on specific areas and visualized with associated heatmaps for IDC, ILC, DCIS, as well as other important features (e.g., TILs, ALI). Therefore, review time was minimal

MISDIAGNOSES IDENTIFIED WITH GALEN

Prostate examples

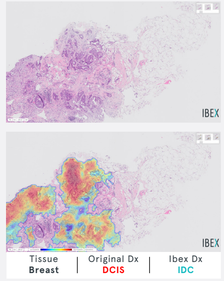


First-ever patient whose cancer was diagnosed by AI. Cancer heatmap shows cancer focus detected by Galen Prostate (high probability areas are shown in red, low probability in blue).

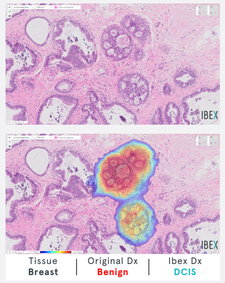


Cancer case revised from G3+3 to G3+4. Gleason heatmap shows G3 in blue, G4 in yellow, G5 in red.

Breast examples



First-ever breast cancer diagnosed by AI. Case was revised from DCIS to invasive ductal carcinoma. Heatmap shows areas identified as IDC (high probability in red).



Missed cancer case identified by the Galen Breast as DCIS. Heatmap shows areas detected by the algorithm as DCIS.

DISCUSSION AND CONCLUSIONS

1. We show here the first **AI-based multi-tissue pathology diagnostic system** ever deployed in routine clinical practice

2. The AI-based QC system was proven to be extremely useful for **increasing diagnostic accuracy** and safety

3. Maccabi now has a solution that delivers very important benefits:
   - AI deployment drove the business case for full digitization of the pathology lab
   - AI support to improve Efficiency (address shortage of pathologists)
   - AI support to improve Quality (alerts and heatmaps for cancer, Gleason, DCIS, etc.)
   - **100% QC on prostate and breast biopsies**