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Development and validation of an artificial intelligence model for detection of gastrointestinal parasites from concentrated wet-mount stool examinations

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Background
Comprehensive diagnosis of gastrointestinal parasites is largely reliant on traditional stool microscopy, despite gains in molecular diagnostics. Permanent stained smear interpretation has been shown by our laboratory to be significantly more sensitive when artificial intelligence (AI) is used to augment slide review. Wet-mount examinations for helminths and protozoa remain a significant challenge for traditional microscopy, digital microscopy, and AI. We developed and validated a deep convolutional neural network (CNN) model that provides highly sensitive detection and presumptive classification of enteric parasites.

Methods
27 different parasites were trained on a CNN model using a wide diversity of 4,049 unique parasite-positive specimens (determined by traditional microscopy) collected in the USA, Europe, Africa, and Asia. Validation data was acquired using a Pramana SpectralHT-2 automated slide scanner. Model validation was performed with a unique holdout set.

Results
In clinical validation, AI correctly detected 250/265 positive specimens (94.3% agreement) and 94/100 negative specimens (94.0%) before discrepant resolution (Table 1). AI also detected 169 additional organisms from the validation specimens that were not previously identified. These additional detections underwent further discrepant analysis to adjudicate the results by scan review and microscopy. After resolution and inclusion of newly defined true positives and false positives, the positive agreement was 428/434 (98.6%). Negative agreement was variable by organism, ranging from 91.8-100% (Table 2). A relative limit of detection study was performed comparing AI to 3 technologists of varying experience using serial dilutions of specimens containing *Entamoeba*, *Ascaris*, *Trichuris*, and hookworm. Known negative stool was used to make the serial dilutions. Technologists were blinded to the study. AI consistently detected more organisms and at lower dilutions of parasites than humans, regardless of the technologist's experience. Reproducibility was assessed using a negative stool, *Taenia*, and *Giardia*. The AI demonstrated 100% precision for the challenge stools.

Conclusions
Use of AI for wet-mount analysis is highly sensitive and detects significantly more organisms than traditional microscopy alone. Use of AI simplifies the parasitology workflow and reduces the reliance on traditional microscopy.

Table 1. Method agreement between conventional microscopy and AI of digitally scanned slides. Agreement values are calculated without resolution of discrepant results (see Table 2 for final analysis). Yellow shading indicates a target that failed to meet validation criteria of 90% agreement.

Organism	Positive Agreement	Negative Agreement
Dientamoeba fragilis	9/10 (90%)	99/100 (99%)
Giardia duodenalis	10/10 (100%)	100/100 (100%)
Endolimax nana	10/10 (100%)	99/100 (99%)
Cyclospora species	10/10 (100%)	100/100 (100%)
Entamoeba hartmanni	10/10 (100%)	99/100 (99%)
Blastocystis species	15/15 (100%)	100/100 (100%)
Chilomastix mesnili	6/10 (60%)	99/100 (99%)
Entamoeba species	10/10 (100%)	99/100 (99%)
Iodamoeba buetschlii	10/10 (100%)	99/100 (100%)
Cystoisospora belli	10/10 (100%)	100/100 (100%)
Balantioides coli	10/10 (100%)	100/100 (100%)
Ascaris lumbricoides	9/10 (90%)	100/100 (100%)
Trichuris trichiura	8/10 (80%)	100/100 (100%)
Hookworm/*Trichostrongylus* sp.	10/10 (100%)	100/100 (100%)
Fish Tapeworm	9/10 (90%)	100/100 (100%)
Taenia species	10/10 (100%)	100/100 (100%)
Enterobius vermicularis	10/10 (100%)	100/100 (100%)
Strongyloides species	9/10 (100%)	100/100 (100%)
Rodentolepis nana	10/10 (100%)	100/100 (100%)
Hymenolepis diminuta	10/10 (100%)	100/100 (100%)
Schistosoma mansoni	10/10 (100%)	100/100 (100%)
Paracapillaria philippinensis	10/10 (100%)	100/100 (100%)
Paragonimus species	10/10 (100%)	100/100 (100%)
Fasciola sp./*Fasciolopsis buski*	10/10 (100%)	100/100 (100%)
Clonorchis/*Opisthorchis* spp.	10/10 (100%)	100/100 (100%)
Schistosoma japonicum	5/10 (50%)	100/100 (100%)
Total Agreement	250/265 (94.3%)	94/100 (94%)

Table 2. Resolved method agreement inclusive of additional organisms detected by the model or during discrepant analysis. Specimens that were ultimately determined to be true-negative after resolution were added to every organism calculation. Organisms in yellow shading failed to meet validation criteria of 90% agreement.

Organism	Positive Agreement	Negative Agreement
Dientamoeba fragilis	11/11 (100%)	101/102 (99.0%)
Giardia duodenalis	25/25 (100%)	102/103 (99.0%)
Endolimax nana	21/21 (100%)	101/105 (96.2%)
Cyclospora species	11/11 (100%)	102/103 (99.0%)
Entamoeba hartmanni	11/11 (100%)	101/102 (99.0%)
Blastocystis species	47/47 (100%)	102/109 (93.6%)
Chilomastix mesnili	12/16 (75%)	101/103 (98.1%)
Entamoeba species	42/42 (100%)	101/112 (90.2%)
Iodamoeba buetschlii	17/17 (100%)	101/103 (98.1%)
Cystoisospora belli	10/10 (100%)	102/102 (100%)
Balantioides coli	13/13 (100%)	102/102 (100%)
Ascaris lumbricoides	16/17 (94.1%)	102/103 (99.0%)
Trichuris trichiura	29/29 (100%)	102/102 (100%)
Hookworm/*Trichostrongylus* sp.	18/18 (100%)	102/102 (100%)
Fish Tapeworm	10/10 (100%)	102/102 (100%)
Taenia species	10/10 (100%)	102/102 (100%)
Enterobius vermicularis	11/11 (100%)	102/102 (100%)
Strongyloides species	15/16 (93.8%)	102/103 (99.0%)
Rodentolepis nana	13/13 (100%)	102/102 (100%)
Hymenolepis diminuta	10/10 (100%)	102/102 (100%)
Schistosoma mansoni	10/10 (100%)	102/102 (100%)
Paracapillaria philippinensis	10/10 (100%)	102/102 (100%)
Paragonimus species	10/10 (100%)	102/102 (100%)
Fasciola sp./*Fasciolopsis buski*	10/10 (100%)	102/102 (100%)
Clonorchis/*Opisthorchis* spp.	10/10 (100%)	102/102 (100%)
Schistosoma japonicum	9/9 (100%)	102/102 (100%)
Misc. Small Protozoans[1]	17/17 (100%)	101/110 (100%)
Total Agreement	428/434 (98.6%)	Variable by target*

*Specimens identified to contain additional organisms were not enrolled as additional negative accuracy specimens and instead were only considered for the target organism identified by AI. As such, overall negative accuracy numbers did not increase for each organism when discrepant resolution was performed. Negative accuracy may increase for specific organisms if false positives were determined after discrepant resolution.

[1]Protozoan trophozoites that could not be further identified without a corresponding trichrome smear. For negative values, objects flagged as miscellaneous protozoans were artifacts or host cells.

References

Mathison BA, Kohan JL, Walker JF, Smith RB, Ardon O, Couturier MR. Detection of Intestinal Protozoa in Trichrome-Stained Stool Specimens by Use of a Deep Convolutional Neural Network. J Clin Microbiol. 2020 May 26;58(6):e02053-19.