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Eureqa™ Helps Researchers to Uncover the True Strength of Ultrasound as a Tool for Detecting Appendix Perforation in Children

For a child with acute appendicitis, the course of treatment depends largely on one question: Has the appendix already burst?

If so, conservative management may be considered. If not, immediate surgery is called for, the goal being to get the appendix out before it bursts. It is therefore critically important that doctors have a quick and reliable way to determine whether a young patient's appendix has already burst.

CT scan has been proven effective in this capacity, but such scans expose patients to ionizing radiation, which can damage DNA and increase cancer risk. For children, that downside is heightened by their greater sensitivity to radiation's effects and by the long lives they have ahead of them within which those effects might develop into cancer. Consequently, CT scan is used as little as possible with young patients.

The most common diagnostic alternative is ultrasound, which doesn't have the resolution required to reveal perforation directly, but which can detect other features of the appendix and the surrounding area that are commonly associated with perforation.

But how effectively can ultrasound discover perforation? And what specific ultrasound findings are most strongly associated with perforation? These are the questions that brought together six clinicians and a statistical modeler for a study that would eventually be published in the May 2013 edition of the American Journal of Roentgenology. The team was led by Dr. Einat Blumfield, radiologist and the Associate Director of Pediatric Radiology at Jacobi Medical Center. Anthony Blumfield, CEO of Radnostics, handled the statistical modeling.

The study looked retrospectively at 161 subjects, ages 1 to 20, who had been diagnosed with acute appendicitis and had undergone ultrasound imaging. In each case, an appendectomy had been performed and, after surgery, the appendix had been determined after surgery to be either perforated or not perforated. The ultrasound images were analyzed and scored with regard to seven features that the team believed were likely to be associated with perforation. Age and gender were also recorded.

Seeking a Model of Unknown Form

Having gathered the required data, the researchers faced a challenge: They didn't know the form of the model they were looking for. "Regular statistical tools (e.g., R-project) are very handy for confirming a model once you have one," says Anthony Blumfield. "They can also help when seeking a model based on data, but this requires a lot of trial and error and a hunch about what you're looking for, especially when correlations are non-linear."

Not having that good hunch, and suspecting nonlinearity, he decided this was a job for Eureqa. At the suggestion of former classmate Hod Lipson, now the director of Cornell University's Creative Machines Lab and an advisor to Nutonian, he had downloaded Eureqa for use in a previous investigation. He therefore knew something of its power and was optimistic as he pasted in the data and started the search.

Eureqa Discovers a Crucial Signal

After just a few hours, Eureqa had produced a striking result — a formula that predicted appendix perforation with about the same level of accuracy as CT scan. And the way Eureqa had achieved that accuracy was equally striking. Anthony Blumfield explains:

"Eureqa divided the subjects into two age groups: under eight, and eight or older. For patients under eight, loss of the ecogenic submucosal layer was associated with perforation. We hadn't defined those categories up front. Eureqa came up with them on its own. When we checked them afterwards with

THE RESEARCHERS

Einat Blumfield [1]
Gopi Nayak [2]
Ramya Srinivasan [1]
Matthew Tadashi Muranaka [3]
Netta M. Blitman, radiology [4]
Anthony Blumfield, statistical modeling [5]
Terry L. Levin [6]

THE JOURNAL ARTICLE

Ultrasound for Differentiation Between Perforated and Nonperforated Appendicitis in Pediatric Patients. American Journal of Roentgenology. 2013; 200:957–962.

The article was honored with selection for the AJR Journal Club.

THE RESEARCH QUESTION

Can ultrasound achieve accuracy levels comparable to CT scan as a tool for differentiating between perforated and non-perforated appendicitis in young patients?

THE CHALLENGE

The target model relating ultrasound findings to perforation was unknown, and (in retrospect) there were important unknown categories within one of the variables.

THE SOLUTION

Eureqa discovered parameters strongly correlated with perforation and revealed the importance of two categories within the age variable. This led to a formula whose application gives ultrasound a level of diagnostic accuracy equal to CT scan in pediatric patients.

THE RESULTS

Doctors can now diagnose perforated appendicitis via ultrasound alone in more cases, thereby reducing the number of cases requiring the exposure to potentially harmful radiation entailed by CT scan.

KEY FEATURES FOR THE RESEARCHERS

- Easy comparison of multiple solutions allowed selection of solutions that were clinically meaningful.

- Adjustable relative importance of different rows of data ("row weighting") allowed the model to be fine-tuned to the desired balance of sensitivity and specificity.

- Expert knowledge could be leveraged to increase search efficiency by excluding mathematical "building blocks" thought unlikely to be a part of the solution.

- A highly intuitive graphical interface provided immediate usability.

NOTES

[1] Department of Radiology, Jacobi Medical Center, Albert Einstein College of Medicine, 1400 Pelham Pkwy S, Bronx, NY 10461. Address correspondence to E. Blumfield. (Einat.blumfield@nbhn.net; Einat_blumfield@hotmail.com).

[2] Department of Radiology, Montefiore Medical Center, Albert Einstein College of Medicine, Bronx, NY.

[3] Department of Radiology, University of Hawaii, Honolulu, HI.

[4] Department of Radiology, Albany Medical Center, Albany Medical College, Scarsdale, NY.

[5] Radnostics, Scarsdale, NY.

[6] Department of Radiology, Children's Hospital at Montefiore Medical Center, Albert Einstein College of Medicine, Bronx, NY.

our regular statistical tests, we found them to be correct, and, in fact, an additional correlation became apparent; we saw that appendicolith [a calcified deposit within the appendix] was also an important predictor of perforation in children under 8. Without Eureqa, it would have been very difficult to discover those age categories or make that subsequent discovery."

While clinicians still take other clinical findings into account, the final result of the study was a simple rule for the interpretation of ultrasound findings: If the ultrasound shows an abcess, or if the patient is under eight years old and ultrasound shows either loss of the submucosal layer or an appendicolith, this strongly indicates perforation of the appendix. This relatively straightforward protocol is already having a signficant impact on clinical practice.

"Since the study, I've had several cases of pediatric patients, younger than 8, with ultrasound findings of an appendicolith and loss of the submucosal echogenic layer," Dr. Einat Blumfield reports. "In these cases I diagnosed perforation, which was confirmed in surgery, while in the past these findings would not have impacted the diagnosis."

Looking Forward: More Parameters, More Accuracy, Even Fewer CT scans

The Blumfields and their fellow researchers aren't satisfied with an ultrasound protocol that merely equals the diagnostic accuracy of CT scan. "We want to look at clinical findings that are associated with perforation such as duration of symptoms, white blood count, and fever," Dr. Einat Blumfield explains. "We'll then use Eureqa to search for a formula that combines ultrasound findings and clinical findings, and we hope to achieve an even higher level of accuracy."

About Eureqa

Eureqa is breakthrough technology that uncovers and explains the intrinsic relationships hidden within complex data. For more information or to get started with a free trial on your desktop or online, visit www.nutonian.com.