Original article

Performance of deep learning in differentiating between distal ureteric calculi and non-calculous calcifications on a KUB radiographs

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Objectives The objective of this study was to evaluate the performance of deep learning (DL) in the differentiation of distal ureteric calculi and non-calculous calcification on kidney, ureter and bladder (KUB) radiographs.

Methods A retrospective review of KUB radiographs of 204 patients with 235 distal ureteric stones and 138 patients with 235 non-calculous calcifications that had been previously identified by investigation, including CT, IVP or URSL, performed at the Department of Radiology, Faculty of Medicine, Chiang Mai University from September 2013 to September 2019. Every calcified density was selected and was cropped into small images. A total of 185 images from each group were randomly selected to be a training dataset and were applied to three pretrained DL networks (AlexNet, GoogLeNet and ResNet50). The remaining 50 images in each group were reserved to be a blind testing dataset. STATA version 14.2 software was used to analyze the sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) and accuracy of each network. Logistic regression was used to calculate the Area Under the Curve (AUC) and the Chi-squared test was used to compare the AUC between the three networks.

Results The sensitivity of the three DL networks was more than 80%, specificity more than 65%, PPV more than 70%, NPV more than 80% and accuracy about 80%. The AUC (95% CI) of the AlexNet network in differentiation of ureteric calculi and non-calculous calcification was 0.79 (0.71-0.87) compared with 0.81 (0.74-0.88) for GoogLeNet and 0.82 (0.74-0.90) for ResNet50 (p = 0.43).

Conclusions DL provides good results in the differentiation of distal ureteric calculi and non-calculous calcification from KUB radiographs. **Chiang Mai Medical Journal 2021;60(3):281-90. doi: 10.12982/CMUMEDJ.2021.25**

Keywords: Distal ureteric stone, Non-calculous calcification, Phlebolith, Deep learning, transfer learning, pretrained network

Introduction

Urolithiasis is one of the most important health issues in Thailand, and has an incidence rate that is rising significantly (1). As most urolithiasis are opaque on kidney, ureter, and bladder (KUB) radiographs but there are some limitations in the detection of calculi as well as the low sensitivity of KUB radiographs, the American College of Radiology (ACR) has suggested that non-contrast CT (NCCT) abdomen and pelvis is the most rapid and accurate technique for evaluating acute onset flank pain where stone disease is suspected, whereas a KUB radiograph has less utility (2-6). However, in Thailand only about 29% of health care institutions have a CT machine and most of those are located in the big city (7). The number of radiologists, important person who can make a more accurate diagnosis of urolithiasis, is also insufficient in Thailand. According to the database of the Medical Council of Thailand in 2019 there were only approximately 2,400 radiologists in the country (8). This resource insufficiency particularly

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Received: February 9, 2021; Revised: April 9, 2021; Accepted: April 19, 2021

affects public hospitals, especially those in suburbs which may not have either high diagnostic machines like the CT or specialist like radiologists.

Artificial intelligence (AI) refers to an intelligent agent that is capable of learning, reasoning, problem-solving and self-developing has been well known worldwide for many years (9). AI has been used in the development of many augmented algorithms used in medical imaging. Deep learning (DL), developed from machine learning (ML), is an image-based algorithm that can analyze input data from image pixels directly without an image segmentation and feature extraction process, and thus can provide more accurate results making it suitable for complicated tasks (10-12). DL has become popular in medical imaging in recent years. It is a powerful image processing tool that can be used in many areas of radiology (11,13). Because of its efficacy, open-source software and the relatively low cost of computer hardware (13, 14), it is possible for healthcare providers to develop DL tools for use in their daily clinical practice.

Among all ureteric calculi, the calculi located in the distal ureter are the most difficult to diagnose because they are located deep in the pelvic cavity and mostly of non-calculous calcification also locate in the pelvic cavity that may mimic calculi, especially phleboliths, the most published pitfall in distinguish from distal ureteric calculi (15,16). To the best of our knowledge, there has been no published data regarding the use of DL to differentiate between distal ureteric calculi and non-calculous calcifications on a KUB radiographs. We believe with the combination of DL, with its low radiation dose and the low cost of KUB radiography, can help physicians in medical centers that do not have a CT machine or a trained radiologist make more accurate diagnoses of calculi. The aim of our study was to evaluate the performance of deep learning in the differentiation of distal ureteric calculi and non-calculous calcifications on a KUB radiographs.

Methods

Patient and Image Acquisition

There were two groups of patients in this study: those with a distal ureteric stone and those with non-calculous calcification in the pelvic cavity. Details of data collection in each group are as follows.

To identify patients with a distal ureteric stone, we conducted a manual search of the database of the Faculty of Medicine, Chiang Mai University, for ICD-10 code N201 calculous of the ureter during the period September 2013 to September 2019. The search identified 2,839 cases of ureteric stones. Our inclusion criteria were patients older than eighteen years with a confirmed diagnosis of distal ureteric stone by at least one diagnostic method, e.g., computed tomography (CT) abdomen/urography/stone protocol, intravenous pyelogram (IVP) or ureteroscopic lithotripsy (URSL). Patients with a diagnosis of proximal or middle ureteric stone were excluded from the study. We enrolled those patients who had a KUB radiograph performed within six months of the diagnosis date which was available for review on the picture archiving and communication system (PACs). The KUB radiographs of these patients had to present radiopaque distal ureteric calculi as determined by consensus of an experienced radiologist in genitourinary imaging and a third-year resident training in radiology during a retrospective review. Any stones non-visualized on a KUB radiograph were defined as radiolucent stones and were excluded from the study. KUB radiographs that had included a retained ureteric stent were also excluded from the study. Finally, there were 204 patients with 235 distal ureteric calculi included in this group.

For patients with a non-calculous calcification in the pelvic cavity, a manual search of PACs for CT urography/stone protocol and IVP was performed in the Department of Radiology, Faculty of Medicine, Chiang Mai University. This process consisted of a backward search beginning with September 2019 and continuing until 235 non-calculous calcifications lesions had been identified, equal to the number of stones in the distal ureteric calculi group. The consensus of a retrospective review of CT or IVP conducted by an experienced radiologist in genitourinary imaging and a third-year radiology resident was used to verify that these images were negative for distal ureteric calculi but did show the presence of other calcifications in the pelvic cavity. Patients that had both a distal ureteric stone and other calcifications in the pelvic cavity in the same investigation were excluded from this group. The KUB radiograph of these patients had to have been performed within six months from the date of the CT/IVP. A total of 235 non-calculous calcifications were obtained from 138 patients.

Ethical approval

This study was approved by the Research Ethics Committee, Faculty of Medicine, Chiang Mai University (Study Code: RAD-2562-06738). For this type of study formal consent of the patient is not required.

Deep learning

DL is an algorithm that uses multilayer computational models resulting in the ability of the algorithm to learn image features and to classify images directly from image pixels. DL with convolutional neural network (CNN) is one of the most popular supervised learning models for learning from labelled data (11-13). The high task accuracy of DL, however, is dependent on massive training data which is expensive, computer-intensive and memory-demanding (17,18). Due to the limits of the data sample in our study, we used the transfer learning method to solve these problems of DL with CNN. Transfer learning allows a CNN to learn from limited training data by transferring knowledge from the a pretrained network of large datasets to the target domain (17,18) (Figure 1). This method preserves only important neurons while removing unimportant neurons, resulting in a smaller sized CNN, thus reducing computational costs while still maintaining the ability to contribute to the target domain without degradation of accuracy (17,18). All the training and testing datasets were applied with three open-source pretrained DL networks: AlexNet (19), GoogLeNet (20) and ResNet50 (21).

Data collection and image analysis

Patients' demographic data, including sex, age, size of the lesion and the diagnostic tests of each patient, were collected.

A total of 342 KUB radiographs (204 from the distal ureteric calculi group and 138 from the non-calculous calcification group) were retrospectively reviewed and combined with CT/IVP/URSL findings to identify and outline the location of every calcification in the pelvic cavity on the KUB radiographs.

Manual selection and cropping of a region of interest (ROI) for each calcification in the KUB radiograph was done with the patient's name and hospital number anonymized (Figure 2). The radiograph of each lesion was cropped to the actual size of the lesion and saved as a Portable Network Graphic (PNG) image and then was re-scaled into 256x256 pixels before being applied to each pretrained DL network.

Input data

The full input dataset of distal ureteric calculi and non-calculous calcifications was comprised

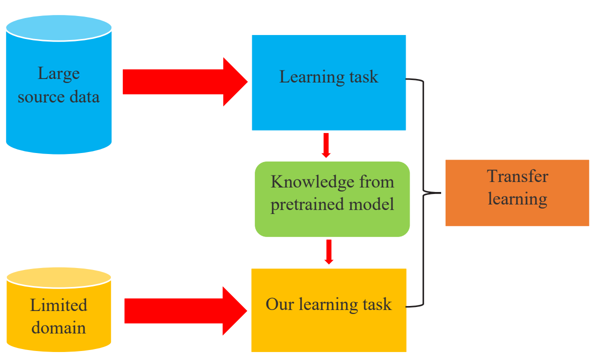


Figure 1. DL with transfer learning process

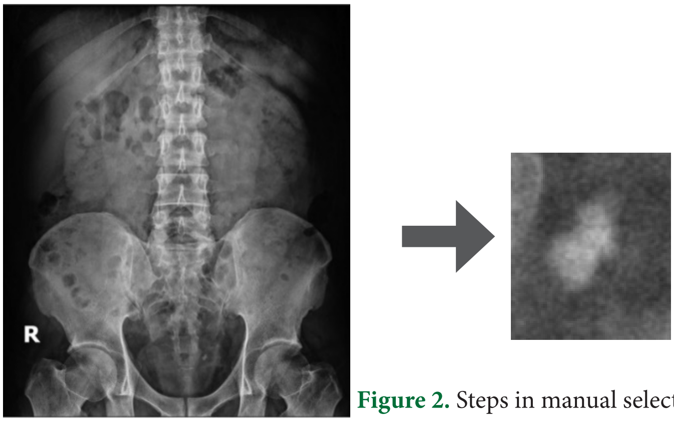


Figure 2. Steps in manual selection and cropping of ROI

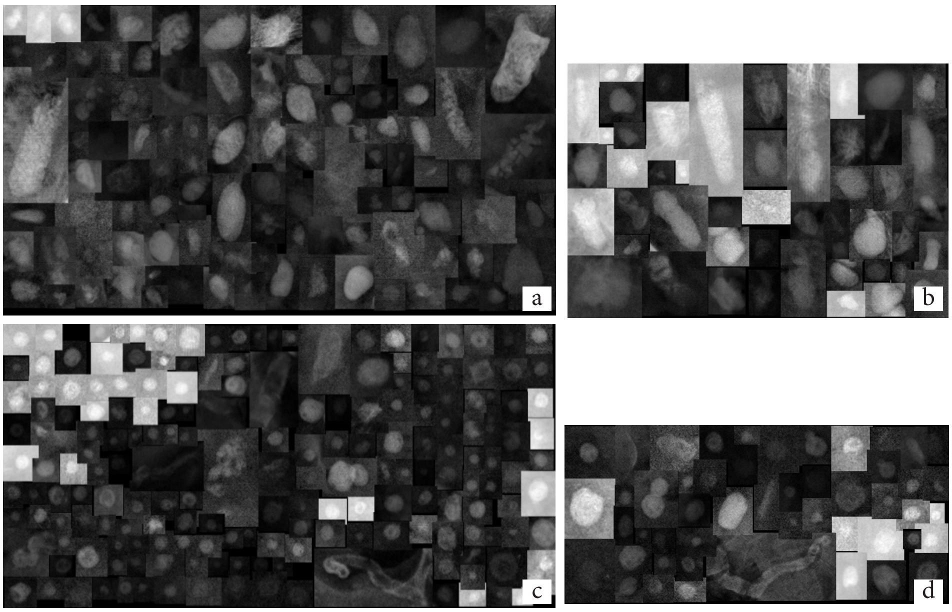


Figure 3. All input datasets were divided into (a) 185 images of distal ureteric calculi for training dataset, (b) 50 images of distal ureteric calculi for blind testing dataset, (c) 185 images of non-calculous calcifications for training dataset, and (d) 50 images of non-calculous calcifications for blind testing dataset

of 470 images, 235 images in each group. The images from each group were computerized and randomly divided into 185 images for the training dataset and 50 images for the blind testing dataset (Figure 3).

First, the 370 images in the training dataset were applied and auto-augmented by each of the pretrained DL networks (AlexNet, GoogLeNet and ResNet50). After that, the 100 images of the testing dataset were applied and adjustment of the parameters of convolutional layers in each DL network was accomplished. Then the training dataset follow with the testing dataset were applied repeatedly to achieve the best satisfied performance in differentiating between distal ureteric calculi and non-calculous calcifications by each DL network. The summarized input data are shown in Figure 4. The parameter settings that resulted in the best performance by each DL network in differentiating distal ureteric calculi and non-calculous calcifications is shown in Table 1.

The performance of the DL in differentiating ureteric calculi and non-calculous calcifications was analyzed for sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) and accuracy using STATA version 14.2 software. The results are reported as percentages. Logistic regression was used to calculate the area

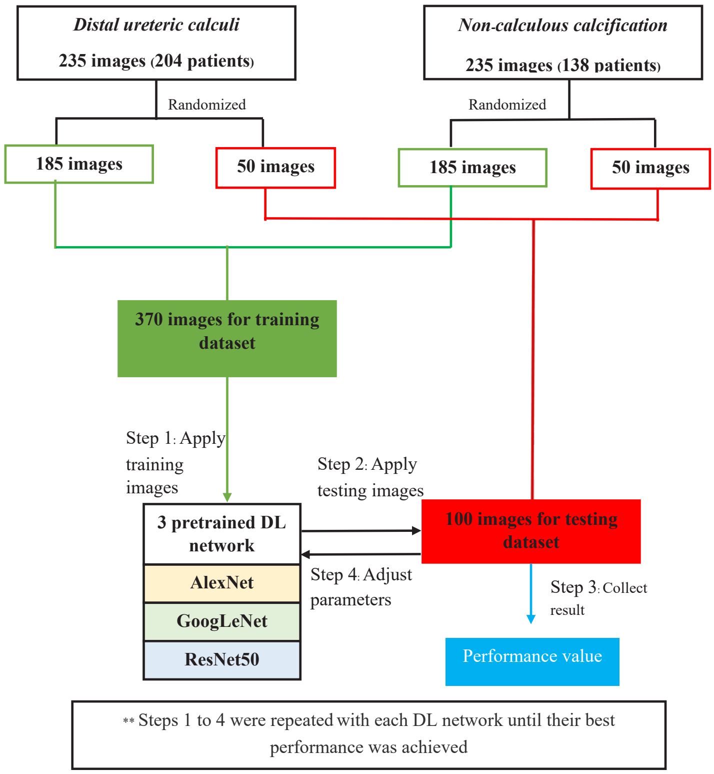


Figure 4. The summarized input data and steps in calculating performance values

Talbe 1. Parameter settings at which each DL network achieved the best performance in differentiating distal ureteric calculi and non-calculous calcifications

Network	Learning rate	Translation (pixels)	Scaling factor	Rotation (degrees)	Max epoch	Mini batch size
AlexNet	0.0001					
GoogLeNet	0.0001	[-10-10]	[0.8-1.2]	[0-360]	20	8
ResNet50	0.00001					

under curve (AUC) and the Chi-squared test was used to compare the AUC among the three DL networks. Results were considered to be statistically significant when the p-value was less than 0.05.

Results

General data

The study included 342 patients with a calcified density in the pelvic cavity as shown on KUB radiographs made between September 2013 and September 2019. There were 204 patients with a confirmed diagnosis of distal ureteric calculi (235 calculi) and 138 patients confirmed as non-calculous calcifications (235 lesions). Our study included both male and female patients, with the number of males higher than females in both study groups. The mean age of the patients in the two groups was not statistically significantly different: 55.9 (± 13.9) years for the patients with distal ureteric calculi and 57.1 (± 13.1) years for the patients with non-calculous calcifications. The minimum and maximum size of lesions in both groups was also not significantly different, with the distal ureteric calculi ranging from 0.31 to 3.80 cm. at the widest diameter, and non-calculous calcifications ranging from 0.20 to 3.15 cm. in the widest diameter. Demographic data of

Table 2. Demographic data of patients

Information	Distal ureteric calculi	Non-calculous calcifications	All
Total patients	204	138	342
Male	120	77	197
Female	84	61	145
p-value	0.012	0.173	19-87 (56.3±13.6)
Age (years)*	19-86 (55.9±13.9)	26-87 (57.1±13.1)	
Size (cm.)	0.31-3.80	0.20 - 3.15	

*Data shown are range (mean and standard deviation)

the patients is shown in Table 2.

There are many types of investigations that can be used to confirm the diagnosis and location of a distal ureteric stone. Confirmation in more than 60% of cases in this study had come from the results of ureteroscopy lithotripsy (USRL) and the rest come from reviewing the CT images. For the non-calculous calcifications group, most of the original confirmations were based on a review of CT images. A summary of the types of investigation used to confirm the diagnoses in each group are shown in Table 3.

Table 3. Type of investigation used to confirm diagnosis of calculi or non-calculous calcification.

Investigation	Distal ureteric calculi (number)	Non-calculous calcifications (number)
IVP	-	8
CT	67	130
URSL	137	-
Total	204	138

DL test results

After training and testing, the datasets were applied to each pretrained DL network including multiple adjustments of the parameters of the convolutional layer in each DL, the results were very satisfactory. AlexNet correctly diagnosed calculi in 44 of 50 lesions and correctly diagnosed non-calculous calcifications in 35 of 50 non-calculi lesions. GoogLeNet correctly diagnosed calculi in 48 of 50 lesions and non-calculous calcifications in 33 of 50 lesions. ResNet50 correctly diagnosed both calculi and non-calculous calcifications in 41 of 50 lesions (Table 4). Each of the pretrained DL networks performed well in differentiating ureteric calculi and non-calculous calcifications. The sensitivity was more than 80% for all three networks, with GoogLeNet the highest at 96%. The specificity was more than 65% for all three networks with ResNet50 the highest at 82%. PPV was more than 70% for all three networks, with ResNet50 again the highest at 82%. NPV was more than 80% for all three networks with the highest being GoogLeNet (94.3%). Accuracy was about 80% with all three networks (range 79-82%). The sensitivity, specificity, PPV, NPV and accuracy of each DL network are shown in Table 5. The AUC (95% CI) of the performance among the three networks in differentiating ureteric calculi

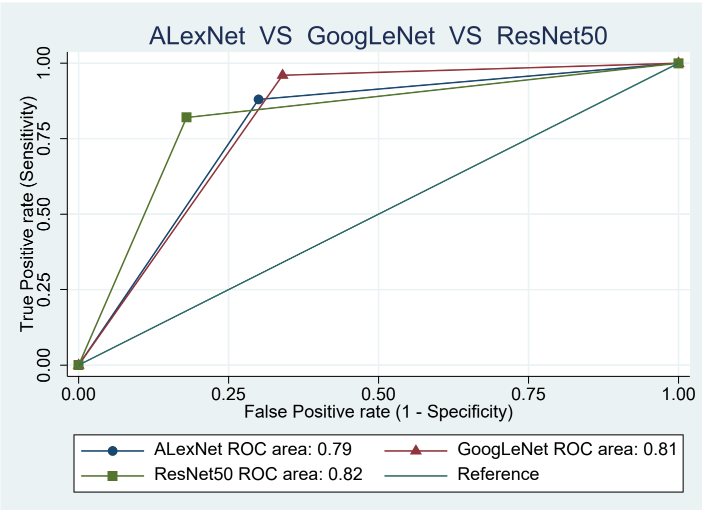
Table 4. Results of each DL model using the test dataset

Network	Character	Stone (number)	Non-stone (number)	Correct (%)
AlexNet	Stone	44	6	79
	Non-stone	15	35	
GoogLeNet	Stone	48	2	81
	Non-stone	17	33	
ResNet50	Stone	41	9	82
	Non-stone	9	41	

Table 5. Performance of each DL network in differentiating ureteric calculi and non-calculous calcifications

Network	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Accuracy (%)
AlexNet	88.0	70.0	74.6	85.4	79.0
GoogLeNet	96.0	66.0	73.8	94.3	81.0
ResNet50	82.0	82.0	82.0	82.0	82.0

Table 6. Area under the curve of each DL network's performance in differentiating calculi and non-calculous calcifications



and non-calculous calcification were not significantly different ($p = 0.43$). The AUC (95% CI) of each network is shown in Table 6.

Discussion

Urolithiasis is one of the most common urologic problems, and its prevalence has progressively increased in Thailand (1). In our study, we found that the incidence of ureteric stones is quite high, nearly five hundred cases per year (2,839 patients over a six-year period). Factors likely related to that increasing prevalence are multifactorial, e.g., changes in social and economic status common to developing countries, an increase in industrial workers, higher average temperatures and increased exposure to sunlight (2,3,15). Another factor could be the increasingly widespread use of CT to evaluate patients with abdominal pain, not only in the emergency room but also in other outpatient units.

Many studies have reported that urolithiasis mostly affects middle aged patients, with the peek incidence occurring in patients between 30-60 years old (1,22). In our study, the mean age of patients with distal ureteric calculi was 55.9 years (range 19-86). That range age in the present study appears wider than in previous publications. One reason could be the longer lifespan of people and the better health care received by younger individuals, including earlier access to the health care services, resulting in more early investigations and early diagnoses.

Urolithiasis usually effects more males than females with ratios ranging from 1.3-5:1 (1,2), similar to our study which found a ratio of 1.4:1 ($p = 0.012$). The non-calculous calcifications had no gender predilection ($p = 0.173$).

Although the number of lesions identified by investigation was equal in the distal ureteric stones group and the non-calculous calcifications group (235), the number of patients was not: there were 204 patients in the former group and only 138 in the latter. This result suggests that multiple lesions are more likely with non-calculous calcifications than with distal ureteric calculi.

DL with a CNN is an effective supervised learning model that can analyze images pixel directly with no need to manually specify the algorithm for geometric parameters that differentiate between calculi and non-calculous calcification as described by Lee (22). However, normally massive training data is needed to the high accuracy task of the DL. Due to the relatively small quantity of training data in our study, the transfer learning method using a pretrained DL network was used. This method allows a CNN to learn from a limited amount of training data without degradation of accuracy (17,18). In our study, we used three well-known open source pretrained DL networks, AlexNet, GoogLeNet and ResNet50, which are not computation-intensive and memory-demanding. By training the networks first before repeatedly testing the datasets, collaborating with the adjusted parameters of each of the pretrained DL networks, the performance of each network in differentiating between ureteric calculi and non-calculous calcifications was quite good. A sensitivity of more than 80% was achieved with each of the networks, higher than the 60% sensitivity of KUB radiographs in stone detection (2,4,5). This result may be due to the ability of DL because all 100 testing images were "new lesions" which the algorithm had never seen before, thus there was no opportunity for an image recognition effect. However, the high sensitivity in our study may also be a result of selection bias as our study included only radiopaque stones, but in actual clinical practice we may be faced with radiolucent stone which would decrease the sensitivity of KUB radiography. In terms of overall performance, applying DL to the KUB radiographs in our study was superior to conventional KUB radiography alone, had comparable performance with the US but was inferior to the performance of CT scans (4,5). The DL method will help alleviate the problem of insufficient availability of high diagnostic radiologic machines as well as of radiologists in non-urban areas of Thailand. Healthcare providers will be able to use this open-source software and low cost computer hardware with KUB radiographs to achieve better performance in ureteric calculi differentiation, resulting in better management decisions for patient care. DL has the potential to continue to develop in the future, further improvement and data input can be served more and more (13). So, we believe that with a larger amounts of input training data become available and newer algorithms of DL are developed, it will result in continued improvement in the performance of the algorithm in the future.

Radiologists should not be afraid of being replaced by DL because, even in a controlled environment, DL can at best only be as good as but not better than humans. In real life the environment is not stable, data may be noisy and atypical patterns may occur (13). Thus, combining algorithms with the knowledge and ability of radiologists will lead to ever better diagnostic accuracy. To that end, radiologists should begin to prepare for the coming era of hybridization between humans and machines.

There were some limitations in our study. First, the training datasets were gathered from a single tertiary hospital and included only a small number of training images. Even though transfer learning allows the use of a small number of training images, giving DL a greater number of training images could potentially improve classification accuracy. Second, the specific features that differentiate between calculi and non-calculi lesions were analyzed directly by DL and thus each of the geographic parameters could not be individually specified. Third, DL can be utilized only when there is a sufficient level of calcification density in the pelvic cavity on the KUB radiograph, and radiolucent stones may result in a false-negative when DL is applied to a KUB radiograph.

In future aspect of this study, more training datasets should be resourced and DL should be developed into a program that can be run on an imaging viewer workstation and can be used with

KUB radiographs to make it easier for radiologists and physicians to make diagnostic determinations.

Conclusions

DL provides good performance in the differentiation between distal ureteric calculi and non-calculous calcifications on KUB radiographs. Further algorithm development with a greater number of training datasets would improve the diagnostic accuracy.

Acknowledgements

We would like to express our sincere gratitude to Asst.prof. Nakarin Inmutto for invaluable help and research advising. Special thanks are extended also to Ms. Sumintra Katib for advice regarding the statistical analysis.

Funding

None

Conflicts of interest

None

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ประสิทธิภาพของการเรียนรู้เชิงลึก (deep learning) ในการแยกระหว่างนิ่วในท่อไตส่วนปลายออกจากหินปูนชนิดอื่น (non-calculous calcification) ที่ปรากฏบนภาพถ่ายเอกซเรย์ของระบบทางเดินปัสสาวะ (KUB radiograph)

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[1]ภาควิชารังสีวิทยา คณะแพทย์ศาสตร์ [2]ภาควิชารังสีเทคนิค คณะเทคนิคการแพทย์ มหาวิทยาลัยเชียงใหม่

วัตถุประสงค์ การศึกษานี้มีเป้าหมายเพื่อศึกษาประสิทธิภาพของ Deep learning ในการแยกระหว่างนิ่วในท่อไตส่วนปลายออกจากหินปูนชนิดอื่นที่ปรากฏบนภาพถ่ายเอกซเรย์ของระบบทางเดินปัสสาวะ

วิธีการ เป็นการศึกษาทบทวนย้อนหลัง ใช้ข้อมูลจากภาพถ่ายเอกซเรย์ระบบทางเดินปัสสาวะของผู้ป่วย 204 รายที่มีนิ่วในท่อไตส่วนปลาย (ทั้งหมดจำนวน 235 รอยโรค) และ ภาพถ่ายเอกซเรย์ระบบทางเดินปัสสาวะของผู้ป่วย 138 รายที่มีหินปูนชนิดอื่นที่ไม่ใช่นิ่วในทางเดินปัสสาวะ (ทั้งหมดจำนวน 235 รอยโรค) รอยโรคทั้งหมดได้รับการวินิจฉัยด้วยการตรวจพิเศษอย่างใดอย่างหนึ่งที่โรงพยาบาลมหาราชนครเชียงใหม่ในช่วงเวลา เดือนกันยายน พ.ศ. 2556 ถึง เดือนกันยายน พ.ศ. 2562 ซึ่งประกอบด้วย CT IVP หรือ URSL รอยโรคทั้งหมดถูกเลือกและครอบตัด (crop) ออกจากภาพถ่ายเอกซเรย์ หลังจากนั้นรอยโรคจำนวน 185 รอยโรคของทั้งสองกลุ่มจะถูกสุ่มออกมาเพื่อใช้เป็นข้อมูลสำหรับการฝึกสอน deep learning ทั้งสามโครงข่ายซึ่งประกอบด้วย AlexNet GoogLeNet และ ResNet50 ส่วน 50 รอยโรคที่เหลือของแต่ละกลุ่มจะถูกใช้เป็นข้อมูลในการทดสอบประสิทธิภาพของ deep learning แต่ละตัว การศึกษานี้ใช้ STATA version 14.2 เพื่อคำนวนหาค่าความไว (sensitivity) ความจำเพาะ (specificity) ค่าพยากรณ์ผลบวก (PPV) ค่าพยากรณ์ผลลบ (NPV) และความถูกต้อง (accuracy) และใช้ logistic regression test เพื่อคำนวนค่า AUC ของ deep learning ทั้งสามเครือข่าย แล้วนำมาเปรียบเทียบกันด้วย Chi-squared test

ผลการศึกษา ค่าความไวของ deep learning ทั้งสามเครือข่ายมีค่าสูงกว่าร้อยละ 80 ค่าความจำเพาะสูงกว่าร้อยละ 65 ค่าพยากรณ์ผลบวกสูงกว่าร้อยละ 70 ค่าพยากรณ์ผลลบสูงกว่าร้อยละ 80 และมีความถูกต้องประมาณร้อยละ 80 พบว่าค่า AUC (95% CI) ของ AlexNet network ในการแยกระหว่างนิ่วในท่อไตส่วนปลายออกจากหินปูนชนิดอื่นที่ปรากฏบนภาพถ่ายเอกซเรย์ของระบบทางเดินปัสสาวะเท่ากับ 0.79 (0.71-0.87) เทียบกับ 0.81 (0.74-0.88) ของ GoogLeNet และ 0.82 (0.74-0.90) ของ ResNet50 (p = 0.43)

สรุป Deep learning ทั้งสามเครือข่ายมีประสิทธิภาพที่ดีในการแยกระหว่างนิ่วในท่อไตส่วนปลายออกจากหินปูนชนิดอื่นที่ปรากฏบนภาพถ่ายเอกซเรย์ของระบบทางเดินปัสสาวะ **เชียงใหม่เวชสาร 2564;60(3):281-90. doi: 10.12982/CMUMEDJ.2021.25**

คำสำคัญ: นิ่วในท่อไตส่วนปลาย non-calculous calcification หินปูนพอกในหลอดเลือด การเรียนรู้เชิงลึก transfer learning pretrained network