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Histopathology

FOLDOSCOPE SCOPE IN NEUROSURGERY A FEASIBLE AND NOVEL TECHNIQUE

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ABSTRACT **Background:** Intra operative squash cytology in identifying CNS lesions and availability of conventional microscope and trained pathologist remains a global health problem especially in remote areas of developing countries which have limited resources .In this study, we evaluated the performance of a low- cost, smartphone attachable paper-based microscope when used for classifying images of Squash cytology of CNS lesions in remote areas and it impact on intraoperative consultation. **Methodology:** Samples collected during operating CNS pathology From Month Of March,2018 To September 2020 Were Included. Total 22 Cases Were Included but 15 cases were operated in our institute. Intraoperative Squash is done at operating table with the sample tissue and images through foldscope were sent to pathologist electronically and time noted to get the result. Same tissue slides images acquired through conventional microscope are compared with images acquired by foldscope. **Results:** Mobile phone-based microscope acquired images were observed and compared with a conventional microscope and found the morphology of the tissue sections was significantly similar to that of conventional light microscope images. The intraoperative time to get the report significantly reduced in remote settings. **Conclusion:** With its clear limitations, improvements can be made to transform it into a cost-effective use device exclusively in the diagnosis of cancer in remote and emergency situations.

KEYWORDS : Foldoscope; Histopathology; Microscopy; Telemedicine.

INTRODUCTION:

High resolution cell phone cameras and microscope lens technology have become widely available and affordable over the recent decade [,]. Despite the significant reduction in the cost of microscope imaging in recent years, many underdeveloped regions of the world still lack the finances to utilize such advances. Smart phones have seen notable technological adaptation, with attachable microscope lenses for smart phone cameras, increasing the magnification of the acquired image, that may rival conventional laboratory diagnostic micro- scopes at a fraction of the cost []. In addition, image editing and processing applications pre-installed on phones allow for immediate manipulation and trans- mission of images. These advancements may offer a more cost-effective solution to the problems of microscopic imaging in the developing world.

Conventional microscope is commonly used for CNS Squash cytology evaluation and trained pathologist is required for the evaluation of the slide. In emergency situations and in rural areas it is not always possible to access for the microscope and pathologist for studying squash cytology evaluation due to resource limitation.

In remote areas, Mobile phone-based microscopy could be one solution to overcome this health sector limitation. In this study we compared the pictures of squash cytology CNS specimen slide taken with a Foldoscope & cell phone and pictures of same slide taken with a traditional microscope and to determine the extent to which foldoscope can be used in squash slide study and to determine its limitations. We studied the amount of time duration we could reduce in studying squash cytology at the operating table by using Foldoscope and to see if mobile phone-based microscopy images could be used in a remote setting where pathologist and conventional microscope are not accessible.

MATERIALS AND METHODS

Study design: Feasibility study.

Samples collected during operating CNS pathology From Month of March to September 2020 Were Included. Total 15 Cases Were Included in The Study.

Sample preparation:

A smear slide was prepared by taking 1-2 millimeters (mm) of the biopsy material with the scalpel blade. Placing the material on a slide and crushing with another slide with just enough pressure to spread the tissue into a thin film in the operation theatre. It was then fixed in 95% alcohol and stained by Haematoxylin and Eosin (H & E). Relevant clinical and radiological data were noted. Raw foldscope paper was open and assembled in order to conduct this study.

Materials: One commercial handheld, portable optical origami types of optical microscope, named "Foldscope" was used to conduct this study. This foldscope was bought from Foldscope instruments, Inc. (San Francis- co, CA). Mobile-phone (Samsung Galaxy S6 edge, Samsung, Korea) was coupled with the foldscope by using tape and magnetic coupler for taking image of the Squash cytology samples (figure 1a). The Foldscope was manually panned and focused according to the guide- line of the manufacturer. Leica DM IL LED (figure 1b) microscope coupled with CMOS camera (IMAGINGSOURCE® DFK 72BUC02) was used to get standard image for comparison with the foldscope obtained images.

Methodology: Raw foldscope paper was open and assembled to conduct this study. After assembly, Squash cytology slides were prepared in operative theater and images were being imaged through Foldscope and mobile phone and images sent electronically to the pathologist. The time taken during intraoperative consultation is noted and compared with conventional method for intraoperative consulation. Then the same slides also being imaged in Leica DM IL LED microscope as reference image and study the limitation of the foldoscope.

Image Processing: All images were saved in JPEG and PNG format, and they are sent to pathologist located at different center.

RESULTS:

22 patients with intracranial tumor and tumor-like lesions were initially enrolled in the study of which seven patients either refused for operative procedure or referred to other centers. Thus, 15 patients were operated at our center and were finally analyzed in the study. Of these, [6 was benign and 9 were malignant] lesions. The different lesions diagnosed are shown in [Table 1] comparing the foldoscope and conventional microscope.

Patients with age range of 14 to 60 years were seen with a male to female ratio of 1.3:1. Patients presented mainly with seizures, headache, nausea, vomiting, vertigo, tinnitus, and difficulty of hearing. some patients presented with local symptoms according to the site of involvement as difficulty in speech, disorientation, paralysis of right side of body, or falling.

Benign lesions were diagnosed in 6 cases, which include pituitary adenoma, Meningioma. Malignant lesions were diagnosed in 9 cases. The cytology features seen through foldoscope were agreeable in only

9 out of 15 cases (Table 2). Intra-operative consultation time interval of diagnosis by squash cytology with foldscope was between 10-12 minutes in 85% of cases and within 15 minutes in all patients when compared to patients getting done in conventional method in remote area. (Table 3)

DISCUSSION

Neurosurgeons often depend upon rapid intraopera- tive diagnosis for immediate surgical management in central nervous system (CNS) lesions. Individuals in developing country at risk for Brain tumours ,which in the majority of cases, lack the resources, infrastructure and/or access to trained pathologists for effective squash cytology screening and intra operative consultation in remote settings.(4) An affordable and easy-to-use diagnostic device could have a significant impact on intra operative squash cytology consultation in this setting, especially in remote areas of developing countries .

High resolution cell phone cameras and microscope lens technology have become widely available and affordable over the recent decade [5,6]. Despite the significant reduction in the cost of microscope imaging in recent years, many underdeveloped regions of the world still lack the finances to utilize such advances.

Foldscope is a low cost, portable, foldable paper microscope. It is invented by Dr Manu Prakash, Assistant Professor from Stanford University, and his PhD student Jim Cybulski. Foldscope is having resolution of 2 micron and magnification up to 140 X. {7}

Naqvi, A et al (8) This study demonstrates that the Foldscope lens has sub- stantial agreement with conventional microscope camera. The accuracy of the Foldscope was 80%, with a sensitivity and specificity of 85 and 90% for the HSIL/Mal category, 80 and 83.3%, for LSIL, and 70 and 96.7% for Normal. Waliullah A S M et al(9) concluded that this method is also feasible for human histopathological sample investigations. In present study out of 15 cases only 9 cases were complete agreement with the three pathologist. partial and inaggrement in this study due to less clarity of cells due to improper preparation of the slide or due to less experience of pathologist in interpreting of slide.

The Squash cytology reports for CNS lesion and intraoperative consultation where slides has to shift to distant area for processing in remote area took more than 30 minutes for the report . By using Foldoscope attached to mobile device could significantly reduce the time to process the reports.Anil et al proved that The mobile devices studied differed, sometimes significantly, in terms of speed and cost.(10)

Even foldoscope images acquired are equalent in quality to that of conventional microscope fine focus is harder with foldoscope. Due to diffraction limit of light the magnification of 2000x cannot be raised anymore. Though the able to study subcellular properties foldoscope high magnification clarity is less than that of compound microscope. It cannot be used in low light setting hence requires LED light source which is provided with foldoscope. Exploration of the slide is difficult because movement and focus adjustment of slide may necessitate need to realign the slide.

The study demonstrated decrease in time consumed for transportation for intra operative consultation and the images acquired are comparable with conventional microscope ,However, during the course of study, few drawbacks were also evident; it includes low contrast and blurring of periphery of the image taken through foldscope in Our study, however, once again confirms the reliability of squash cytology study through foldoscope and further multicenter study with larger number of patients may help to decide its use in clinical practice.

CONCLUSION:

Requirement of knowledge squash slide preparation and squash cytology knowledge, along with improvement of device is required to improve the sensitivity of the study. with its clear limitations, improvements can be made to transform it into a cost-effective use device exclusive in the diagnosis of cancer in remote and emergency.

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Conflict of Interest: None.

Fig 1a Foldoscope after assembly and attached to phone coupler

Fig 1b Conventional Microscope with magnetic

Table 1.Images Of Various CNS Pathology Under Foldoscope And Conventional Microscope

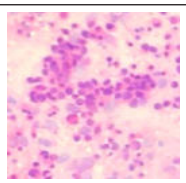
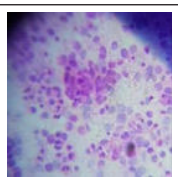
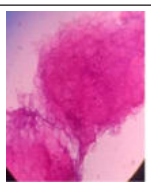
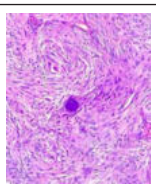
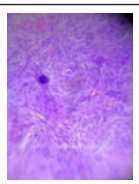
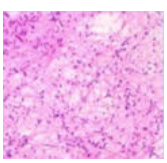
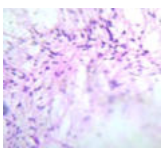
	400X MAGNIFICATION MICROSCOPE	140X MAGNIFICATION FOLDOSCOPE WITH 5X ZOOM
HIGH GRADE GLIOMA		
EPIDERMOID		
MENINGIOMA		
LOW GRADE GLIOMA		

Table 2 Tumour Identification And Diagnosis By Various Pathologist Comparing With Microscopic Diagnosis.

MICROSCOPE IMAGE DIAGNOSIS	FOLDOSCOPE IMAGE DIAGNOSIS (PATHOLOGISTS=3Members) COMPLETE AGREEMENT	PARTIAL AGREEMENT	DISAGREEMENT
GBM (4 cases)	3		
GLIOMA (3cases)	3		

CEREBELLAR HEMANGIOBLASTOMA. (1case)		1	2
MENINGIOMA (5cases)		1	2
EPIDERMOID (2cases)	3		

Table 3: Time Duriation For Arrival To Conclusion By Pathologist Located At Various Places From The Hospital

Average Time Taken At Each Hospital To Convay Diagnosis	Foldoscope / At Hospital	500M From Hospital	2KM From Hospital
GBM (4 cases)	8-10MIN	20-25MIN	<30MIN
MENINGIOMA (5cases)	10-15MIN	25MIN	<30MIN

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