

# THE DESIGNING OF A BIOINFORMATICS MICROSCOPE TO OBSERVE BIOPSY CANCER CELLS USING AN IMAGING PROCESSING SYSTEM VIA MEDICAL WEB SERVICES

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## ABSTRACT

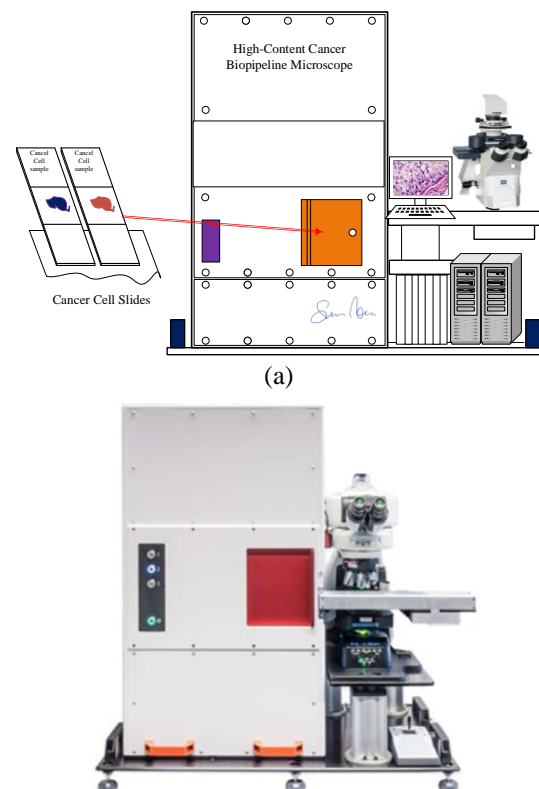
This research aims to apply knowledge in biomedical engineering and computer engineering to examine tissue cells to distinguish cancer cells from normal cells, thereby helping to facilitate the increase in safety of cancer diagnostic specialists who do not need to go to the hospital to diagnose biopsies amid the COVID-19 situation. This study can be developed further in the future. This research was developed on a personal portable computer using an Intel Core i7-9750H processor, 16.0 GB of memory, and a Geforce RTX2060 GPU, and using Visual Studio Code, Android Studio, and Pycharm to process it. It uses the principle of image classification which uses images obtained from an electronics microscope with a magnification of 400x[1]. Then it will be adjusted to be suitable for processing before being put into image processing by changing the size of the image subsequently the image is converted to grayscale, and make the grayscale images are black and white images. Then the images are taken for processing and the cancer cells are classified by using techniques to change the shape or outline of the image (Morphological Operations) before finding the borders of the cancer cells. The borders are displayed via web services, using a smartphone as a communication tool to send all the images such as cancer cells photos and cancer cells videos to the destination physician.

**Keywords:** Bioinformatics microscope, Visual Studio, Android Studio program, Image Classification, Morphological Operations, Biopsy cancer cells.

## 1. INTRODUCTION

Prior to the coronavirus disease 2019 (Covid-19) incident in the world, specialist physicians had to take a look at the biopsy samples using a microscope in a hospital every day. The coronavirus disease 2019 incident makes it difficult for those doctors to come to the hospital for the fear of contacting the disease. In addition there is an inevitable need to come to the big operation, which the doctor will not be able to avoid. In this paper, an example of the detection of cancer abnormalities in addition to the cytology examination are presented methods for detecting

abnormalities through microscopy which looks through the camera making it possible to see the lesion more clearly than the naked eye. To lead to biopsy of suspected abnormalities, pathological examination for final diagnosis shall be made and the diagnosis must be completed within 24 hours. However, if the hospital were to procure such a system (Figure 1), it would be an exorbitant investment because the price of the automatic biopsy scanner is very expensive (approximately 600,000 USD). Therefore, the research team of Srinakharinwirot University has joined to design and develop a prototype of a bioinformatics microscope for transmitting real-time images of cancer biopsy samples online to solve problems for medical personnel.



**Figure 1.** (a) Structure and (b) Fully cancer biopsy sample scanner.

Figure 1 is a fully automatic cancer biopsy scanner system based on the principle of operation[2]. Initially clinical staff has to take biopsy samples from suspected cancer patients and place them in slide holders as shown in Figure 2(a). Then the samples are put them in the slide

holder 120 the slide is called the classes box, as shown in Figure 2(b). The system then loads all slides containing the cancer biopsy samples onto the biometrics microscope by conveyor belts and sends the images to the physician at the next destination as shown in Figure 4.



**Figure 2.** (a) Slide glass for biopsy cancer cells and (b) Classes box containing biopsy cancer cells slides.

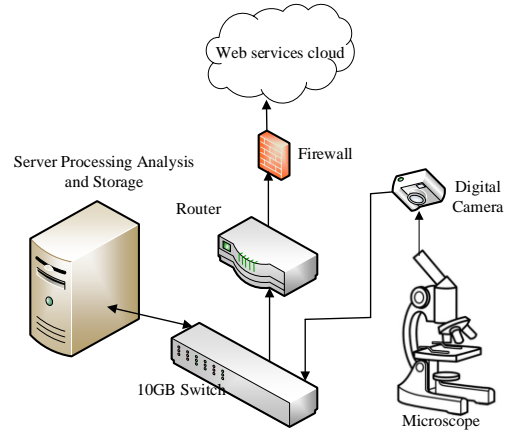


**Figure 3.** Biometrics microscope body for scanning biopsy cancer cells samples.

## 2. DESIGN STRUCTURE OF SYSTEM

### 2.1 The first part of Network Structure Design

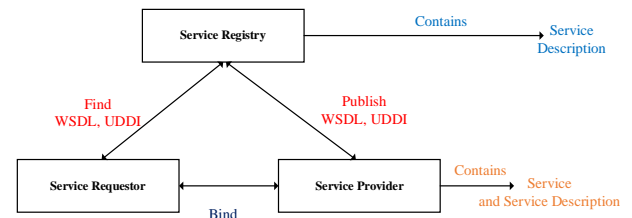
The overall system structure consists of four parts: firstly, the network structure, followed by the second architecture of web service, the third is the image analysis, and finally, the dedicated server. The network structure as shown in Figure 4 consists of a biometrics microscope, an ethernet switch that supports a 10Gb/s bandwidth, a router, dedicated server, firewall security and web services cloud[6]. The server device is responsible for storing biopsy cancer cells imaging obtained from a biometrics microscope as the data can be saved directly to the server, meaning that multiple users (physician specialists) can view the patient's data getting new images continually while the system is busy. Similarly, the server can automatically process and analyse the images or video signal on the designed location when the data is placed there.



**Figure 4.** The network structure of the microscope image transmission system to the physician's destination.

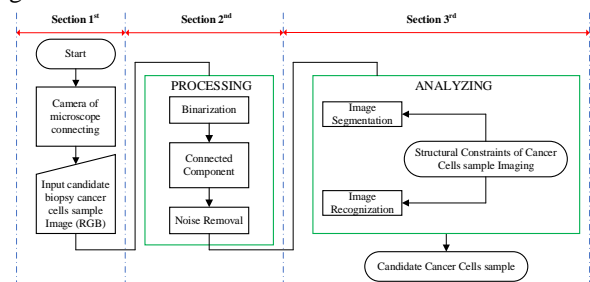
A firewall is a device that serves to control access between an external network that may not be secured and an internal network that need to protect against, which can be a router, computer, or network. The network can be combined depending on the method of management.

The architecture of web service consists of three roles which are firstly, the service provider, secondly, the service requester, thirdly, service registry. The interaction consists of three operations publishing finding, and finally binding. These operations and roles act upon the artifacts of web services. The architecture of web service is shown in Figure 5.



**Figure 5.** The architecture of web service.

The image of cancer cells sample analysis of this research consists of three sections[3]. Firstly, it is the cancer cells imaging input from the microscope to the communication system. Secondly, the processing section consists of binarization, connected components, and a noise removal box diagram. Finally, the analysis section consists of image segmentation, image recognition, and structural constraints of cancer cells sample as shown in Figure 6.

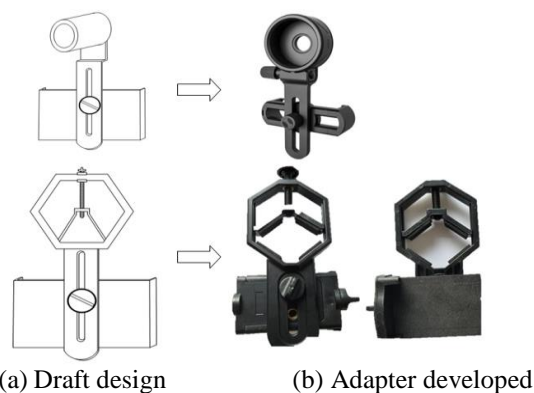


**Figure 6.** The flowchart of image analysis.

The dedicated server will be processing analysis and storage image/video data from the microscope at the source in the hospital through a 10GB internet switch. The ethernet switch serves as a collection of the cancer cell's imaging signal received from the server for transmission on the cloud for communication with the terminal computer by transferring the high-rate data transfer from the workstation to a specialized server using that 10 GB connection.

## 2.2 The second part of hardware structure design

This part is the design of the mounting structure for digital cameras and smartphones. The smartphone adapter was used to attach two types of microscopes as shown in Figure 7, but only one was developed for this research as shown in Figure 7 to suit the smartphones used in the experiment.



(a) Draft design (b) Adapter developed  
**Figure 7.** The structure of smartphone adapter.

A optical lens suitable for this research was selected by choosing a 70 mm diameter lens to cover a microscope as shown in Figure 8.



**Figure 8.** The optical lens suitable for this research.

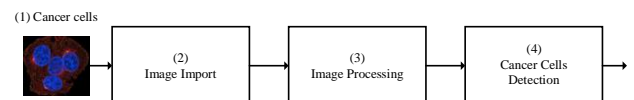
For the biometrics microscope, was selected a microscope with a magnification of about 400x to change the image to be suitable for the image processing software as shown in Figure 9.



**Figure 9.** A microscope with a magnification of 400x used in research.

## 3. IMAGE DATA IMPORT SYSTEM DESIGN

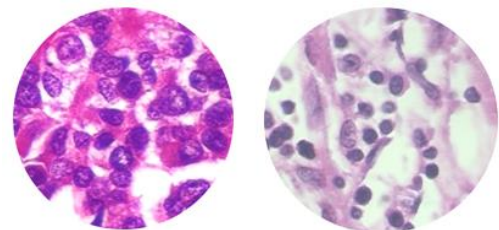
The process of differentiating or filtering cancer cells using image processing is divided into 3 main parts. These are (1) Cancer cells (2) Image import, (3) Image preprocessing, (4) Cancer cells detection at 400x - 600x magnification of the microscope. The processing section is powered by an Intel® Core™ i7 processor. -8300H with a clock frequency of 2.30GHz and 16 GB of main memory on windows 10/64-bits block diagram is shows in Figure 10.



**Figure 10.** The process of identifying cancer cells.

### 3.1 Importing image data from a microscope

Importing image data from a microscope is the process of obtaining images in digital form from a digital camera. The image was taken under a microscope using the magnification of a 400x lens and was a dot bmp image for processing to identify cancer cells in breast cancer cases, as shown in Figure 11.

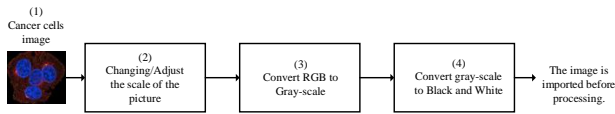


**Figure 11.** Cancer cells sample image.

### 3.2 Image pre-processing.

Image pre-processing is used to improve the image and prepare in order to make the image suitable for detecting

cancer cells. There are three steps: (1) Cancer cells image, (2) changing/adjusting the image resolution (3) converting the image to grayscale (4) converting the grayscale image to black-and-white image as shows in Figure 12.



**Figure 12.** Image pre-processing.

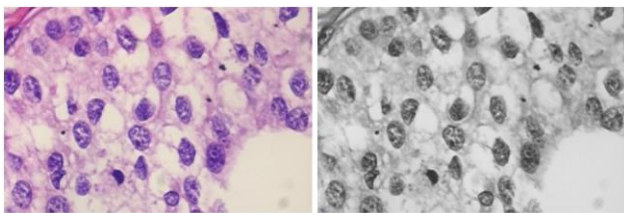
### 3.3 The Image Resolution Adjustment

The process of reducing the resolution of the image being processed was done because the images data received from each digital camera has a different resolution. In some cases, the image data has high resolution making the image size too large. This results in a delay in the image processing. It is necessary to adjust the size to be in the matching format. The process of adjusting the image resolution reducing the image size.

The process of resizing images to reduce image input data size is required because the processed images have different resolutions. Also, in some cases the image data have very high resolution, resulting in the processing have taking too much time as mentioned above. As a result, the resolution of the processed image is set to 760x600 pixels[3].

#### 3.3.1 Converting an image to grayscale

The process of converting an RGB image to grayscale is done because images in the RGB color system consist of multiple levels of color which makes it difficult to separate cancer cells from the background. In order to easily get the cancer cells separated from the normal cells and the cancer cells from the background the conversion is shown in Figure 13.

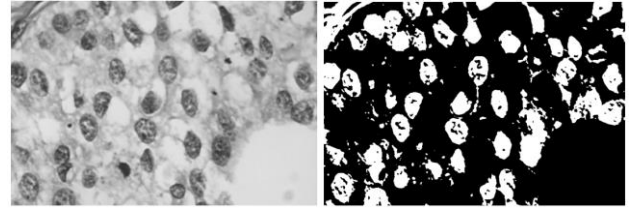


**Figure 12.** The output cancer cells image is converted from RGB into grayscale.

#### 3.3.2 Converting cancer cells image from grayscale to black and white

The process of converting grayscale images into black and white uses the thresholding-invert technique by Otsu method to make the image edges of cancer cells prominently separated from the normal cell background. This makes the image pixel values having two levels of data, the number value of '0' and '255'. By the way, the number value '255' is displayed as a white tone, and the value of '0' is black using a thresholding technique. It

makes the object separated clearly from the background as shown in Figure 13.



**Figure 13.** The output cancer cells image is converted from grayscale into black and white.

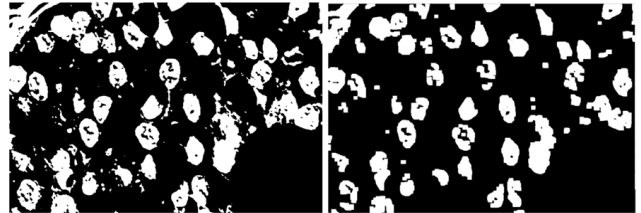
### 3.4 The magnification image process of 400x for identifying cancer cells

#### 3.4.1 Morphological operations

This process causes the shape of the object in the image to change due to the black and white image obtained has not been able to identify cancer cells and contains unwanted parts. This process has three steps which are removing unwanted parts within the image, enlarging the object suspected to be cancer cells and the filling the internal spaces.

#### 3.4.2 Removing unwanted parts.

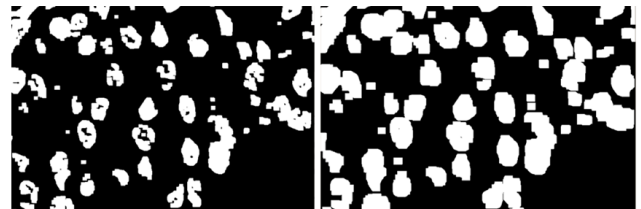
This step is to remove unwanted part within the image and take the black and white image obtained from threshold-invert by the Otsu method to perform morphological operations as opening by using a marked size equal to 10 x 10, the result is shown in Figure 14.



**Figure 14.** The resulting image is obtained by Morphological operations opening type.

#### 3.4.3 Magnifying objects suspected to be Cancer cells

Having removed the unwanted image by morphological operations using dilation using a marked size of 10x10, the result is shown in Figure 15.

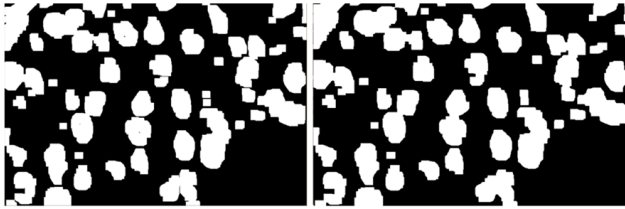


**Figure 15.** The resulting image is obtained by Dilation Morphological operations (Open).



#### 3.4.4 Filling the empty spaces within the object

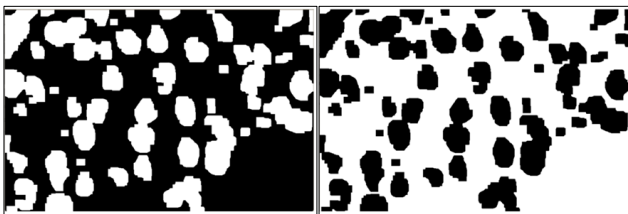
An enlarged image of an object that is suspected to be cancer cells is taken and processed with closing Morphological operations using mark size 5 x 5, the result is shown in Figure 16.



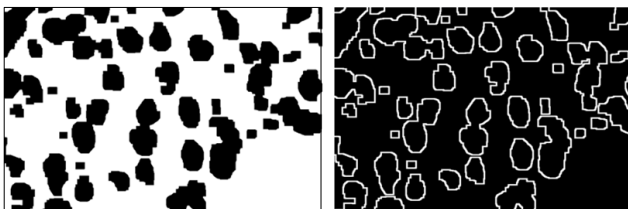
**Figure 16.** The resulting image of filling in the padding with Morphological operations method (Closing).

#### 3.4.5 Cancer cells image edge line finding

After obtaining an image that fills the object gap, it is converted to the RGB image in order to find out the edge line as shown in Figure 17. Subsequently, it will check for the circumference of the object in the image as the edge line is caused by the difference in light intensity from one point to another point. If this difference is a large value, the edge line is cleared, if the value is small the edge line will not be cleared[3]. The edge line finding is a measure of the change in light intensity[4]. The edge line is obtained using the Gradient method, which is to find the edge line by finding the lowest and highest points in the form of the first derivative of the image. Due to the edge line will be in the part above the threshold value using the marked size equal to 5 x 5 the result is as shown in Figure 18.



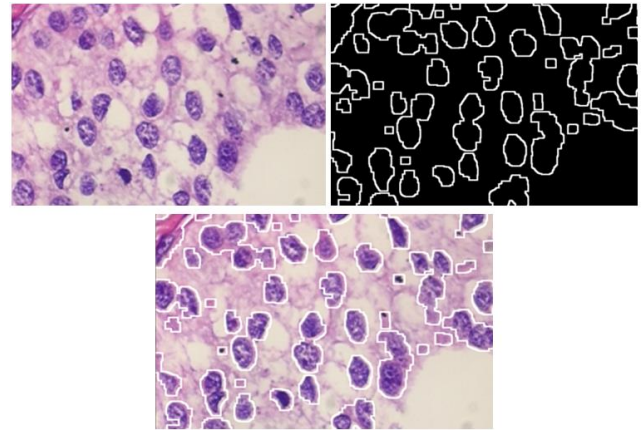
**Figure 17.** The image colour is inverted.



**Figure 18.** The image of returning edge line using the gradient method.

#### 3.4.6 The edge display to classify cancer cells

Having found the border of the experimental object, it will be displayed on the sample image to identify the location of the cancer cells. The result is shown in Figure 19.

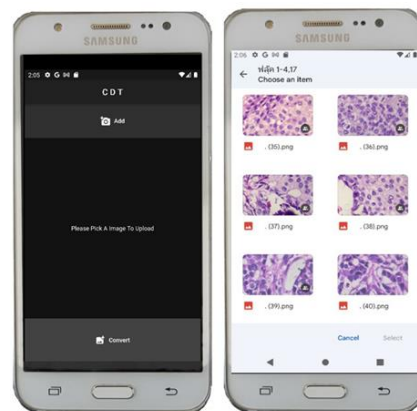


**Figure 19.** The image of cancer cells classification results.

### 3.5 The User Interface

#### 3.5.1 The output display

Figure 20 (a) is the window of the program consisting of the following components: (1) Image data input section, (2) Image data display section, (3) Image analysis process, and (4) the Image data display section that is analyzed.



**Figure 20.** Components of the overall user interface.

#### 3.5.2 Image data input

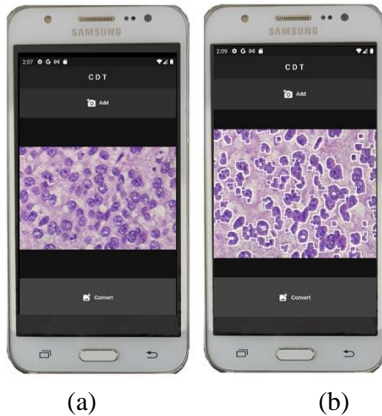
Cancer cells image data can be improved from within the smartphone to display, which will look like a button for pressing as shown in Figure 20 (b). After the selected cancer cell's image data are selected, the application on a smartphone will display the selected image data as shown in Figure 21.

#### 3.5.3 The image analysis process

In this section, the selected image is imported from the smartphone and sent to the server, after which it will be taken into the image processing to detect cancer cells and send it back to the image display. There is a button for pressing to operate as shown in Figure 22.



**Figure 21.** The cancer cells image is displayed in the image data obtained from a microscope via a smartphone.



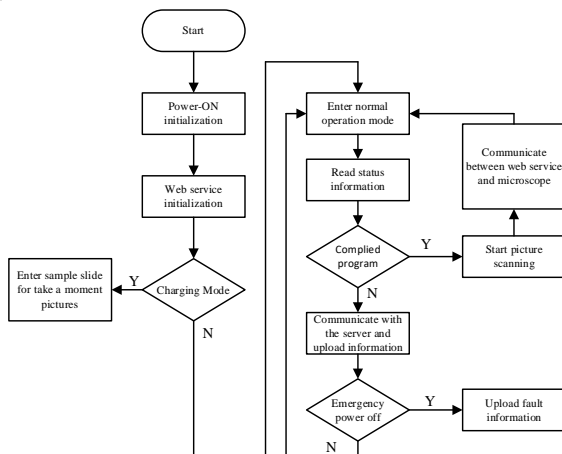
**Figure 22.** (a) The image of cancer cells before analysis and (b) successfully analysed.

### 3.6 Software Application Design

Software application design consists of three parts: (1) The part of the image processing obtained from the microscope. (2) The part of communication between microscopes. (3) The part is display software on smartphones or notebooks.

#### 3.6.1 Principles of application design

There is the following flowchart as shown in Figure 23.



**Figure 23.** Flowchart of Image analysis of biopsy cancer cells samples and communication between microscope and smartphone.

#### 3.6.2 Program code for obtaining variables from a microscope

The program code is written for obtaining variables and mobile communication to web services are as follows:

```

/*
This program code is use in the SWU Research in 2021-2022
*/
#include <Simple DTH.h>; Preparing the sample
#include <Wire.h>
#include <CCD.h>
// CCD = 2
Int print CCD = 2;
Simple CCD ccd12(pin CCD)
//CCD2
Int ccd2=A1 ;
Int ccd=0 ;
//CCD1,2 ;
Void setup ( ) {
Serial.begin (19200) ;
//CCD12
ccd12.int( ) ;
If (ccd12.isValidID( ))
Serail.println (Error-please check the CCD1 and 2) ;
{
Void loop ( ) {
//CCD12
Byte pixel = 0 ;
Byte resolution = 0 ;
Int err = Simple CCDErrSuccess ;
If (( err = ccd12.read (&pixel, &resolution, NULL)) != SimpleCCDErrSuccess)
{
Serial.print ("read CCD1 failed, err =") ;
Serial.print ("read CCD1 Code( err)) ;
Serial.print ("read CCD2 failed, err =") ;
Serial.print ("read CCD2 Code( err)) ;
Serial.print (" , ") ;
Serial.println (SimpleCCD12ErrDuration(err)) ;
Delay (1000) ;
Return ;
}
//CCD12
CCD12 = analogRead (CCD12) ;
Serail.print ("pixel=") ;
Serail.print ("CCD=") ;
Serail.print ("resolution=") ;
Serail.print ((int) resolution) ;
Serail.print (CCD1.get image()) ;
Serail.print ("C") ;
Serail.println (" " ) ;
Delay (1500) ;
}
}

```

#### 3.6.3 The image analysis program code from the microscope

The program code is written for image analysis is follows:

```

/*

```

This program code is use in the SWU Research in 2021-2022.....This step to preparing and import the cancer cells sample, changing the color of digital image.

```

*/
import 'dart:convert';
import 'dart:io';
import 'package:http/http.dart' as http;
import 'package:flutter/material.dart';
import 'package:image_picker/image_picker.dart';
void main() {
  runApp(MyApp());
}
class MyApp extends StatelessWidget {
  const MyApp({Key? key}) : super(key: key);
  @override
  Widget build(BuildContext context) {
    return MaterialApp(
      debugShowCheckedModeBanner: false,
      title: 'Flutter Demo',
      theme: ThemeData(
        primarySwatch: Colors.cyan,
      ),
      home: MyHomePage(
        title: ('CDT'),
      ),
    );
  }
}
class MyHomePage extends StatefulWidget {
  const MyHomePage({Key? key, required this.title}) :
    super(key: key);
  final String title;
  @override
  State<MyHomePage> createState() =>
    _MyHomePageState();
}
class _MyHomePageState extends State<MyHomePage> {
  File? selectedImage;
  String? message = "";
  String? url;
  uploadImage() async {
    final request = http.MultipartRequest(
      "POST", Uri.parse("https://731c-101-109-109-170.ngrok.io/uplod"));
    final headers = {"Content-type": "multipart/form-data"};
    request.files.add(http.MultipartFile('image',
      selectedImage!.readAsBytes().asStream(),
      selectedImage!.lengthSync(),
      filename: selectedImage!.path.split("/").last));
    request.headers.addAll(headers);
    final response = await request.send();
    http.Response res = await
      http.Response.fromStream(response);
    final resJson = jsonDecode(res.body);
    setState(() {
      message = resJson['message'];
    });
  }
}

```

```

Future getImage() async {
  final pickedImage =
    await ImagePicker().getImage(source:
    ImageSource.gallery);
  selectedImage = File(pickedImage!.path);
  setState(() {
    message = "";
  });
}

```

```

@override
Widget build(BuildContext context) {
  return Scaffold(
    appBar: AppBar(
      backgroundColor: Colors.grey[900],
      title: Text(
        "C D T",
        style: TextStyle(color: Colors.white),
      ),
      centerTitle: true,
    ),
    body: Container(
      child: Column(
        children: [
          Container(
            color: Colors.grey[850],
            width: double.maxFinite,
            height: 80,
            child: Row(
              mainAxisAlignment: MainAxisAlignment.center,
              children: [
                TextButton.icon(
                  icon: Icon(
                    Icons.add_a_photo,
                    color: Colors.white,
                  ),
                  label: Text(
                    "Add",
                    style: TextStyle(color: Colors.white),
                  ),
                  onPressed: getImage,
                ),
              ],
            ),
            Expanded(
              child: Container(
                alignment: Alignment.center,
                color: Color.fromARGB(255, 19, 18, 18),
                child: selectedImage == null
                  ? Text(
                      "Please Pick A Image To Upload",
                      style: TextStyle(color: Colors.white),
                    )
                  : message != ""
                    ? Image.network(message!)
                    : Image.file(selectedImage!)),
              Container(
                color: Colors.grey[800],
                width: double.maxFinite,

```

```

height: 100,
child: Row(
  mainAxisAlignment: MainAxisAlignment.center,
  children: [
    TextButton.icon(
      icon: Icon(
        Icons.add_photo_alternate,
        color: Colors.white,
      ),
      label: Text(
        "Convert",
        style: TextStyle(color: Colors.white),
      ),
      onPressed: uploadImage,
    ),
  ],
),
),
),
),
),
);
}
}

```

### 3.6.4 Program code for communication between the Microscope and smartphone

The program code is written for mobile communication to web services as follows:

```

/*
Development of Development of Biopipeline Microscope
Using Imaging Processing System via 4G/5G Technology.
Created 2022 : By Assoc.Prof.Dr.Suranan Noimane,
Modified on 16 April 2022
This program code is step to preparing communication
system to web services.
*/
#include <SoftwareSerial.h>
  softwareSerial sim8001(0, 1);
  #define button 7
  bool button_State;
  void setup ( )
{
  pinMode (Button 1, INPUT_PULLUP);
  sim8001.begin (9600);
  serail.begin (9600);
  delay (1000);
}

  void loop ( )
{
  button_State = digitalRead (button 1);
  if (button_State == Low) {
    serail.println ("Button Pressed");
    delay (200)
    send image ( ) ;
  }
}

```

```

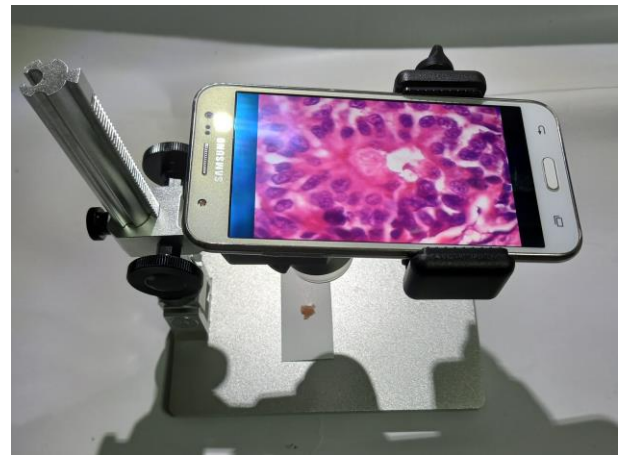
}
  if (sim8001.available ( )){
    serail.write (sim8001.read ( ));
  }
}

void Send image ( )
{
  serail.println ("Sending Image.....")
  sim8001.print ("AT+CMGF=1\r");
  delay (100);
  sim8001.print
("AT+CMGS=\r"+910080659745\r"r");
  delay (500);
  sim8001.print ((char26));
  delay (500);
  sim8001.println ( );
  serial.prontln ("Image Sened.....");
  delay (500);
}

```

### 3.7 The program execution

For the analysis testing, image processing, and communication with smartphones, the application has to be installed on the smartphone via the APK program for Android to be completed before the next step. The specialist physician who wishes to analyze images obtained on a smartphone will need to install an application program called "Microscope.apk" before being connected to the microscope[5]. The program is chosen by selecting the image from the camera, after which it will be able to use in real-time immediately as shown in the figure. 24 – Figure 28

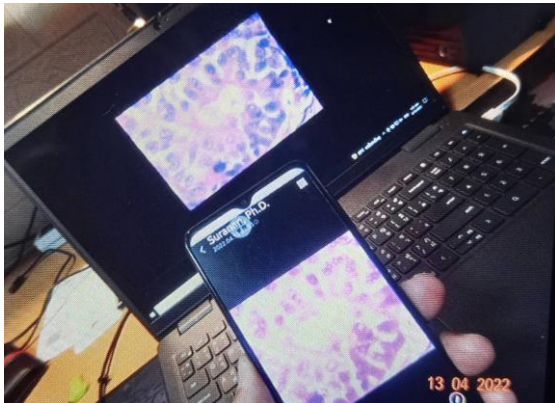


**Figure 24.** The cancer cells were imaged from a microscopic to a smartphone.





**Figure 25.** The cancer cells were imaged from a microscopic to a smartphone (continue)



**Figure 26.** The cancer cells were imaged from a microscopic to a smartphone (continue)



**Figure 27.** The cancer cells were imaged from a microscopic to a smartphone (continue)



**Figure 28.** The cancer cells were imaged from a microscopic to a smartphone (continue)

#### 4. RESULTS

A prototype of bioinformatics microscope to observe biopsy cancer cells using imaging processing system via medical web services was designed and developed using a Python and Java Programming Language. The results of the evaluation of the efficiency of the cancer cell classification algorithm are as follows:

There are two evaluation criteria: First evaluation criterion is Sensitivity (SS) which is a numerical value indicating the likelihood of cancer cells being counted by a specialist and a computer program. The sensitivity is calculated from equation (1). If the value of cancer cells is low, the program user will need to count more cells in large numbers. The second evaluation is Positive predictive value (PPV) which refers to a numerical value that indicates the probability of cancer cells being counted by a computer will be counted similarly by a specialist.

The predicted positive value is calculated from Equation (2). If the value is low, the program user must subtract a large number of cells.

$$SS = \frac{TP}{TP + FN} \quad (1)$$

$$PPV = \frac{TP}{TP + FP} \quad (2)$$

Where

The value of TP (True positive) means the number of cells that the algorithm can exclude from the background match the experts identified as cancer cells.

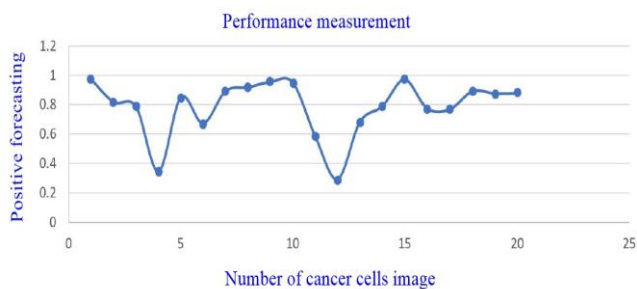
The value of FN (False negative) refers to the number of cancer cells that the algorithm cannot rule out from the background but which experts identify as cancer cells.

The value of FP (False positive) or false positive Refers to the number of cancer cells that the algorithm can rule out from the background but experts do not identify as cancer cells.

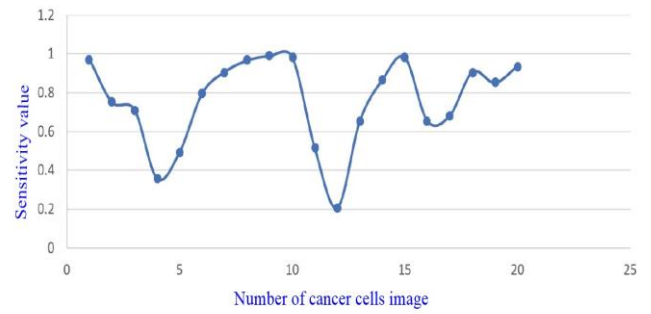
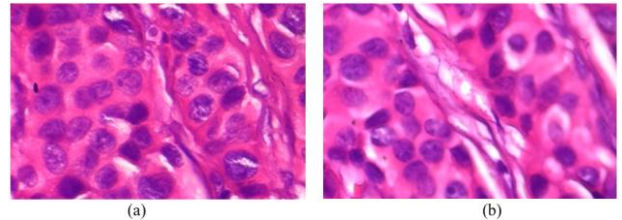
**Table 1** The cancer cells efficiency classification.

No.	TP	FN	FP	SS	PPV
1	69	2	2	0.971831	0.971831
2	36	12	8	0.75	0.818182
3	37	15	10	0.711538	0.787234
4	10	18	19	0.357143	0.344828
5	34	35	6	0.492754	0.850000
6	35	9	17	0.795455	0.673077
7	58	6	7	0.90625	0.892308
8	56	2	5	0.965517	0.918033
9	84	1	4	0.988235	0.954545
10	58	1	3	0.983051	0.95082
11	17	16	12	0.515152	0.586207
12	7	27	17	0.205882	0.291667
13	30	16	14	0.652174	0.681818
14	45	7	12	0.865385	0.789474
15	102	2	3	0.980769	0.971429
16	51	27	15	0.653846	0.772727
17	60	28	18	0.681818	0.769231
18	106	11	13	0.905983	0.890756
19	57	10	8	0.850746	0.876923
20	72	5	10	0.935065	0.878049
The average value				0.75843	0.783457

Table 1 is the cell count values detected as cancer cells where the mean SS is 0.75843 and PPV is 0.783457 which is plotted as a graph as shown in Figure 29 and Figure 30.

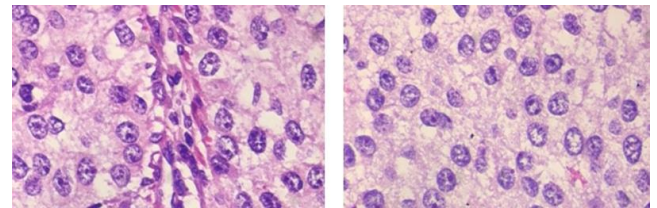
**Figure 29.** Performance measurement graph.

The results of the cancer cells evaluation of the effectiveness classification. The results of the twenty cancer cells image classification efficacy evaluation results (Fig. 30 – Fig. 35) are shown in Table 1. The efficacy is 75.84% sensitivity and 78.34% positive prognostic value, which was quite high. The program user will add or delete a small or very small number of cells.

**Figure 30.** Sensitivity measurement graph.

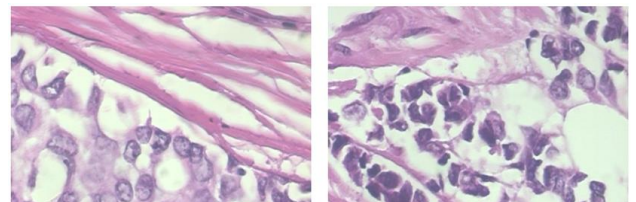
(a) Image cells before classification

(b) Image cells after classification

**Figure 31.** The cancer cells type 1<sup>st</sup>

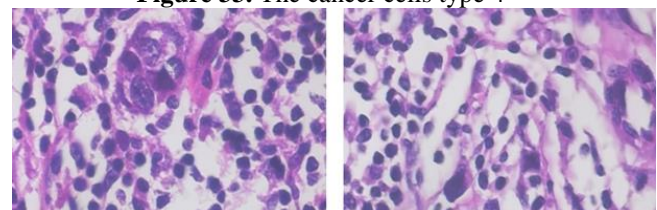
(a) Image cells before classification

(b) Image cells after classification

**Figure 32.** The cancer cells type 3<sup>rd</sup>

(a) Image cells before classification

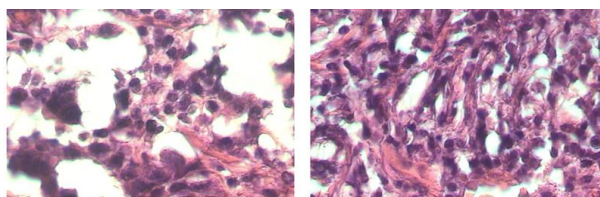
(b) Image cells after classification

**Figure 33.** The cancer cells type 4<sup>th</sup>

(a) Image cells before classification

(b) Image cells after classification

**Figure 34.** The cancer cells type 5<sup>th</sup>



(a) Image cells before classification (b) Image cells after classification

**Figure 35.** The cancer cells type 8<sup>th</sup>

## 5. CONCLUSION

The author has designed a prototype of bioinformatics microscope devices for special physicians and a comprehensive analysis has been conducted using special software on smartphones. The results of the work have shown that this design demonstrated the reliability and stability of biometrics system requirements, verifying the rationality of this structured design. The way of using special software to conduct an analysis and check for designing work is simple, practical, highly efficient, solutions to the production cycle, and reduces the research and development costs. In this way this method is worthy of further extension to improve this bioinformatics microscope for future work in this field.

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