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Diagnostic Capabilities of a Smartphone-Based Low-Cost Microscope

Abstract: Microscopy enables fast and effective diagnostics. However, in resource-limited regions microscopy is not accessible to everyone. Smartphone-based low-cost microscopes could be a powerful tool for diagnostic and educational purposes. In this paper, the imaging quality of a smartphone-based microscope with four different optical parameters is presented and a systematic overview of the resulting diagnostic applications is given. With the chosen configuration, aiming for a reasonable trade-off, an average resolution of 1.23 µm and a field of view of 1.12 mm^2 was achieved. This enables a wide range of diagnostic applications such as the diagnosis of Malaria and other parasitic diseases.

Keywords: Smartphone-based Microscope, Diagnostics, Malaria, Parasites, Neglected Tropical Diseases (NTDs)

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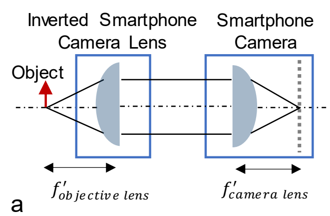
1 Introduction

Microscopy is an important tool for science and medicine. As a diagnostic method, it is considered the gold standard for numerous diseases. However, in many resource-limited regions, microscopy equipment is not available. Smartphone-based low-cost microscopes have the potential to enable microscopy diagnostics in these regions. Currently, smartphones are very abundant and there will be an estimated number of 6.4 billion smartphones in the world by 2021 [1]. Additionally, the integrated smartphone camera systems have improved significantly in recent years, resulting in the possibility of developing high-resolution smartphone-based microscopes with an advanced but low-cost optical system. To be an adequate replacement for conventional laboratory microscopes the resolution of a smartphone-based microscope has to be sufficient to enable a wide range of diagnostic applications.

Several smartphone-based microscopes have already been developed [2, 3]. The approach of Switz et al. [2] is based on an additional inverted smartphone camera lens in front of the smartphone (see Fig. 1a). This type of optical system allows cost-effective microscopy with a relatively high resolution and a large field of view (FOV). Consisting out of two lenses, the magnification of this setup can be calculated by Eq. 1, shown in Fig. 1. Since the focal length of both lenses is in the same order of magnitude, there is no or only limited optical magnification. However, since the sensor of a smartphone has a higher number of pixels than its screen, the image can be digitally magnified if full resolution information is needed.



a

$$M = -\frac{f'_{objective\ lens}}{f'_{camera\ lens}} \quad (1)$$

b

Figure 1: (a) Optical principle of the smartphone-based microscope; (b) Eq. (1) to calculate the optical magnification.

In this work, a smartphone-based low-cost microscope with an inverted smartphone camera lens and a monolithic focusing mechanism is used [4]. It is crucial that the smartphone-based microscope achieves a high resolution to enable a wide range of diagnostic applications. Various studies showed that the diagnosis of some diseases is already possible [5, 6]. In this work, the highest possible resolution without changing the requirements of the used smartphone was determined and a systematic overview of the diagnostic applications of the smartphone-based microscope is provided.

2 Materials and Methods

2.1 Optical System

A smartphone-based microscope developed previously [4], is used to determine the potential applications. To evaluate what

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resolution is achievable, four different lenses, taken from smartphone camera modules, are tested in the smartphone-based microscope frame (Fig. 2a). The lenses were taken from smartphone models from Apple (Apple Inc., Cupertino, CA, US) and Samsung (Samsung Electronics Co. Ltd., Suwon, KR) (see Table 1). Four different lenses with different focal lengths, $f'_{objective\ lens}$, were tested to verify if a shorter focal length results in a higher optical magnification and therefore in a higher resolution.

Table 1: Used smartphone camera lenses and their properties.

Smartphone	Module	Focal length [mm]	Cost [€] Inc. tax
iPhone 5S	rear camera	4.12	2.99
iPhone 7	front camera	2.89	11.99
iPhone 5S	front camera	2.15	2.90
Samsung Galaxy S4	front camera	1.9	2.39

2.2 Verification of the Optical System

To determine the resolution of the system, images of a test target were recorded with four different configurations of the smartphone-based microscope. The test target used was a MIL-STD-150A US Air Force optical resolution test target (see Fig. 2b).

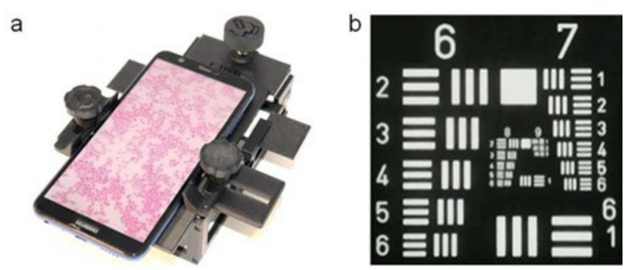

Figure 2: (a) Smartphone-based microscope [4] (b) US Air Force optical resolution test target.

Nine state of the art smartphones, all released after 2015, were used to take images of the test target with each smartphone-based microscope. This resulted in nine images per microscope configuration. To determine the resolution of each smartphone-based microscope the contrast gradient of every element in group 8 of the test target is analysed. An element is considered resolved when the Michelson contrast was at least 10 % in both, horizontal and vertical orientation. With the smallest resolvable element, the arithmetic mean of the Michelson contrast was calculated for each smartphone-based microscope. In order to determine the FOV, images of a 1 mm calibration target were taken. Using the recorded calibration target size, the FOV was determined by referring to the pixel size of the respective smartphone.

2.3 Diagnostic Applications

A literature research was performed focusing on diseases that can be diagnosed by conventional light microscopy. This investigation provided information about the potential diagnostic applications of the smartphone-based microscope. The structural sizes of the pathogens or physiological structures were determined in order to compare to the resolution achieved by the microscope. Initially, the different diseases which had already been imaged with a smartphone-based microscope were collected. In addition, diseases that are common in resource-limited regions were selected by using the World Health Statistics 2018 of the World Health Organization (WHO) [7]. Lastly, the diseases were filtered by those in which a diagnosis with the achieved smartphone-based microscope resolution was possible. The search engines GoogleScholar and Pubmed were used to find the publications.

3 Results

3.1 Resolution and Field of View

The resulting resolutions and the respective FOV of the lenses of different focal lengths are shown in Table 2. The highest individual resolution was achieved by using a Xiaomi Mi 8 Lite smartphone (Xiaomi Inc., Beijing, China) and the lens of the Samsung Galaxy S4 front camera. This configuration results in element 6 of group 8 being resolvable, which corresponds to a spatial resolution of 1.1 µm. Furthermore, the Samsung Galaxy S4 lens provided the highest resolution on average, with the nine different smartphones used.

Table 2: Average optical magnification (M, see Eq. 1), mean minimal resolved element of group 8, resolution and field of view (FOV) of the different smartphone-based microscope configurations, when using nine different state of the art smartphones.

Smartphone module	Ø M	Element (group 8)	Resolution [µm]	FOV [mm²]
iPhone 5S (rear)	-1	1	1.95	16.87
iPhone 7	-1.38	2	1.74	4.9
iPhone 5S (front)	-1.86	4	1.38	1.2
Samsung Galaxy S4	-2.11	5	1.23	1.12

3.2 Diagnostic Applications

26 different diseases were found that could be diagnosed by light microscopy and whose pathogens size enables a diagnosis with a smartphone-based microscope with a resolution of 1.23 µm or better. The potentially diagnosable diseases are listed in Table 3.

Table 3: Overview of the diseases potentially diagnosable with the smartphone-based microscope without using immersion fluid and the respective pathogen structure size. Diseases marked with an asterisk are classified as an NTD. If only one dimension is given for the size, the pathogen usually has a long and slender shape.

Disease	Specimen	Size [µm]	Ref.
Malaria	Blood smear	1.5×1	[8]
Taeniasis*	Stool sample	30	[9]
Enterobiasis	Skin scraping	50×20	[10]
Fasciolosis*	Stool sample	60×117	[11]
Intestinal fluke infections*	Stool sample	130	[12]
Opisthorchiasis*	Stool sample	30×12	[13]
Paragonimiasis*	Sputum sample	80	[14]
Loiasis	Blood smear	290×7.5	[15]
Lymphatic filiariasis*	Blood smear	250×10	[16]
Mansonelliasis	Blood smear	1.5×100	[17]
Onchocerciasis*	Skin biopsy	220×5	[18]
Ascariasis*	Stool sample	60×40	[19]
Trichuriasis*	Stool sample	50×22	[20]
Schistosomiasis*	Stool sample	83×60	[21]
Hookworm disease*	Stool sample	64×36	[22]
Strongyloidasis*	Stool sample	6-13	[23]
Chagas disease*	Blood smear	6-20	[24]
Human African trypanosomiasis*	Blood smear	10×40	[25]
Amoebiasis	Stool sample	10-20	[26]
Balantidiasis	Stool sample	≤150	[27]
Giadiasis	Stool sample	9×5	[24]
Leishmaniasis*	Skin biopsy	1.8-2	[28]
Scabies*	Skin scraping	300×250	[29]
Sickle cell anemia	Blood smear	7.5	[30]
Iron deficiency anemia	Blood smear	7.5	[30]
Hematuria	Blood smear	7.5	[30]

Fig. 3 shows an example of specimen images of the diseases Malaria, human African trypanosomiasis, Trichuriasis and Taeniasis taken with the smartphone Huawei P10 (Huawei Technologies Co., Ltd., Shenzhen, China) and using the lens of a Samsung Galaxy S4 front camera.

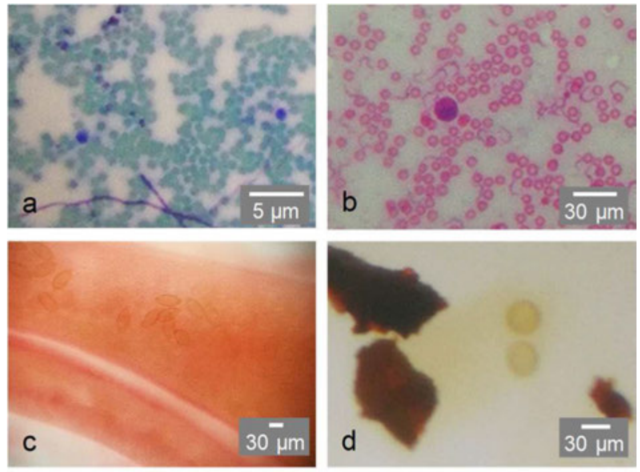

Figure 3: Images taken with transmitted illumination with the smartphone-based microscope of a giemsa stained blood smear with erythrocytes infected with malaria plasmodium (bluish) where an accumulation of stain due to a crack in the cover plate can also be seen (a), a giemsa stained blood smear infected with microfilarie causing human African trypanosomiasis (b), a stool sample infected with eggs of the Trichuris Trichiura causing Trichuriasis (c), and a stool sample infected with eggs of Taenia saginata causing Taeniasis (d).

4 Discussion

The use of the Samsung Galaxy S4 front camera lens resulted in the highest resolution. This increase of resolution compared to the use of the other lenses is accompanied by a significant reduction of the FOV. This reduction has a negative effect on the sensitivity of a diagnosis.

However, only with this higher resolution, the widespread disease Malaria (pathogen size 1.5 µm) is diagnosable. This is especially significant given the fact that there were an estimated 216 million cases worldwide causing approximately 445,000 deaths in 2016 [7], of which the majority occurred in resource-limited regions. Additionally, a variety of diseases that are categorised as neglected tropical diseases (NTDs) cause serious problems in the same regions with 1 billion infected people worldwide and an estimated number of 534.000 deaths per year. The reason for the neglect of this diseases is often a lack of financial resources [31]. An overall number of 16 NTDs are diagnosable with the described smartphone-based microscope. Especially a high number of parasitic diseases are diagnosable e.g. helminths and protozoal infections. On the other hand, pathogens with structural sizes below the resolution limit as e.g. mycobacteria may be too small to resolve properly. The digital magnification allows to zoom in without steps which enables the diagnosis of diseases requiring a hierarchy of magnifications. Compared to a conventional microscope the costs are remarkably low with manufacturing costs under 10 € [4] and low-cost storage and shipping due to the compact size and light weight. However, it should be noted that laboratory equipment for specimen preparation can create additional costs. Therefore, the use of a low-cost smartphone-based microscope is especially beneficial for diagnosing parasitic worms since due to the preparation possibilities of many stool samples without any laboratory equipment no further costs occur. In contrast, for the remaining diseases, laboratory equipment is needed for specimen preparation.

Furthermore, in comparison to a conventional microscope, the resolution of the smartphone-based microscope is sustainably limited. This can lead to a less reliable diagnose regarding specificity and sensitivity. However, as a first test it is potentially useful. Overall, the use of a smartphone-based microscope provides the ability of diagnosing a wide range of diseases that particularly affect resource-limited regions.

Author Statement

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