MAYA Antiviral Sticker: Medical & Scientific Data

Date: 8th May 2020

The MAYA Sticker was developed in the Technion Israel Institute of Technology and is manufactured by DYKAM, Kibbutz Ein Harod Meuhad, Israel.

Severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) is the strain of coronavirus that causes coronavirus disease 2019 (COVID-19), a deadly respiratory illness. As described by the U.S. National Institutes of Health (U.S. NIH), SARS-CoV-2 is a positive-sense single-stranded RNA virus and is the successor to SARS-CoV-1. It is contagious in humans, and the World Health Organization (WHO) has designated the ongoing pandemic of COVID-19 a Public Health Emergency of International Concern.

Epidemiological studies estimate each infection results in 1.4 to 3.9 new ones when no members of the community are immune and no preventive measures taken. The virus primarily spreads between people through close contact and via respiratory droplets produced from coughs or sneezes. It mainly enters human cells by binding to the receptor angiotensin converting enzyme 2 (ACE2).

Based on the low variability exhibited among known SARS-CoV-2 genomic sequences, the strain is thought to have been detected by health authorities within weeks of its emergence among the human population in late 2019. The virus subsequently spread to all provinces of China and to more than 150 other countries in Asia, Europe, North America, South America, Africa, and Oceania. Human-to-human transmission of the virus has been confirmed in all these regions. On 30 January 2020, SARS-CoV-2 was designated a Public Health Emergency of International Concern by the WHO, and on 11 March 2020 the WHO declared it a pandemic.

As of 19th May 2020, there have been 320,454 deaths and 4,911,720 Coronavirus confirmed cases worldwide, while the proportion of infections that result in confirmed cases or progress to diagnosable disease remains unclear.

There is no doubt that non-pharmaceutical countermeasures are of extreme importance in order to delay and mitigate the impact of SARS-CoV-2.

The MAYA Sticker is a single-use device for the improvement of the antiviral protection of surgical masks and other soft face-covers.

The MAYA Sticker is affixed to a surgical mask, providing extra protection against infections carried by airborne droplets or aerosol particles. These airborne particles, wet or dry, may carry

viruses, transmitted as a result of emitted droplets through coughing, sneezing, breathing, raising of dust, spraying of liquids, toilet flushing, etc.

The MAYA Sticker activity is based on three mechanisms of action:

a) Improved filtration of aerosols and saliva droplets by means of low nanometric pore-diameter and low porosity. The pores are in order of magnitude of tens to hundreds nanometers, versus tens to hundreds of microns in standard surgical masks.

b) Capture of the viruses due to the unique chemical-physical properties of the fiber and the multilayer structure of the sticker.

c) Inactivation (neutralization) of the viruses trapped in the sticker by the biocidal material.

The MAYA Sticker is composed of a support layer of nonwoven microfibers, polymer nano-fibers fabric integrated with the well-known widely used disinfectant povidone iodine (PVP-I). All materials are FDA approved.

The MAYA Stickers are manufactured by employing state-of-the-art 3D print technology that allow to create this porous but firm fabric, that allows free breathing without any burden on the user on the one hand, while preventing viruses to enter the user's trachea.

The MAYA Sticker is adhered to the surgical mask by thin layer of adhesive material . Upon hitting the MAYA Sticker, the droplet is absorbed into the nanofiber fabric and the pathogens are trapped in the nanofibers, while the disinfectant, PVP-I, then inactivates the viruses.
Several trials were performed to evaluate the efficacy and tolerability of the MAYA Sticker by leading hospitals, medical centers and scientific institutes in Israel, under the permission and approval of the various governmental ministries of the State of Israel.

Content

1. The MAYA Sticker: structure & characteristics

The pore size is in the range of 60 – 1,000 nm, thickness, L_1~ 20 µm, wherein said porosity allows air permeability, k between $10^{-7}k/L_1$ to $10^{-5}k/L_1$ [m].

The dimensions of the MAYA Sticker: 110 mm x 150 mm x 0.45 mm (7.425 cm^3). The nanofibers of nonwoven fabric are integrated with 3.8625 mg of povidone iodine, PVP-I[1],[2],[3] per unit, equal to 234 mg/m^2. The structure of the MAYA Sticker is illustrated in Fig. 1 below.

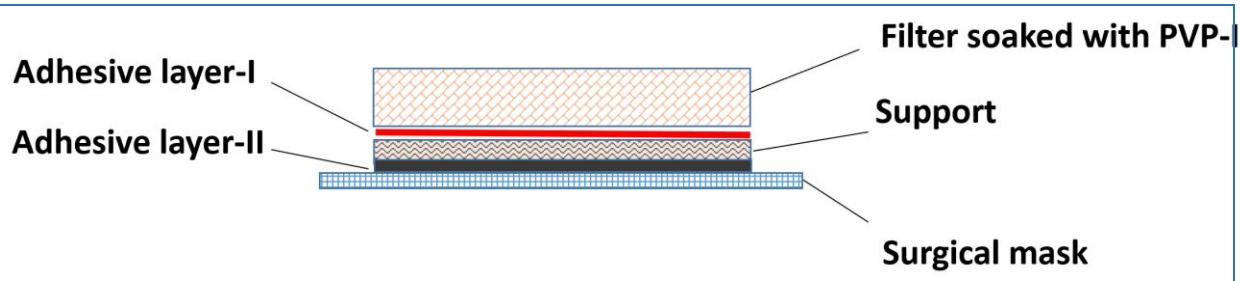

Fig. 1. MAYA Sticker – structure.

Optical images of a surgical mask with and without the MAYA Sticker are presented in Fig. 2 and Fig. 3 below, respectively. Optical images of the MAYA's nanofiber network with PVP-I are presented in Fig. 4 and Fig. 5, respectively.

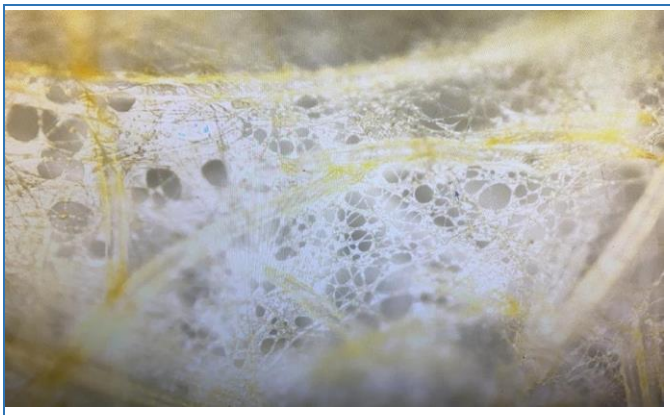

*Fig. 2. Optical image of the surgical mask **with** the MAYA Sticker (scale bar: 200 µm).*

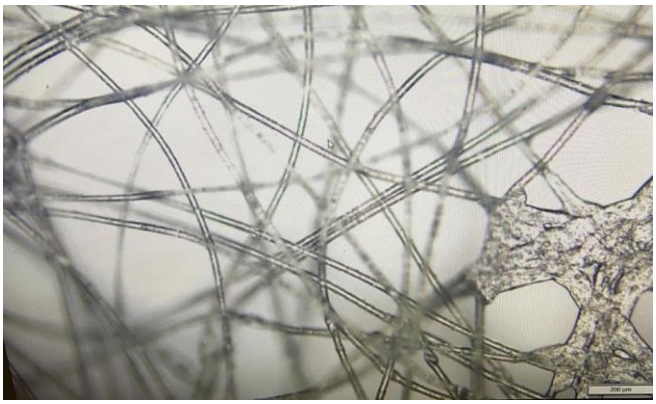

*Fig. 3. Optical image of the surgical mask **without** the MAYA Sticker (scale bar: 200 µm).*

1 Kampf et al., Persistence of coronaviruses on inanimate surfaces and their inactivation with biocidal agents, *J. of Hospital Infection* 104 (2020).

2 Eggers et al., Rapid and Effective Virucidal Activity of Povidone-Iodine Products Against Middle East Respiratory Syndrome Coronavirus (MERS-CoV) and Modified Vaccinia Virus Ankara (MVA), *Infect Dis Ther* (2015).

3 Kariwa et al., Inactivation of SARS Coronavirus by Means of Povidone-Iodine, Physical Conditions and Chemical Reagents, *Dermatology* (2006).

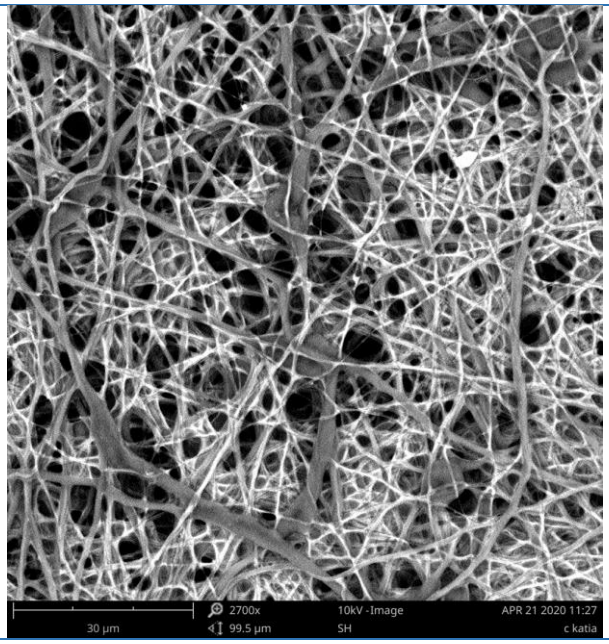

*Fig. 4. Scanning Electrons Microscopy (SEM) image of the nanofiber network **with** PVP-I (scale bar: 30 µm).*

*Fig. 5. Optical image of the nanofiber network **with** PVP-I (scale bar: 50 µm).*

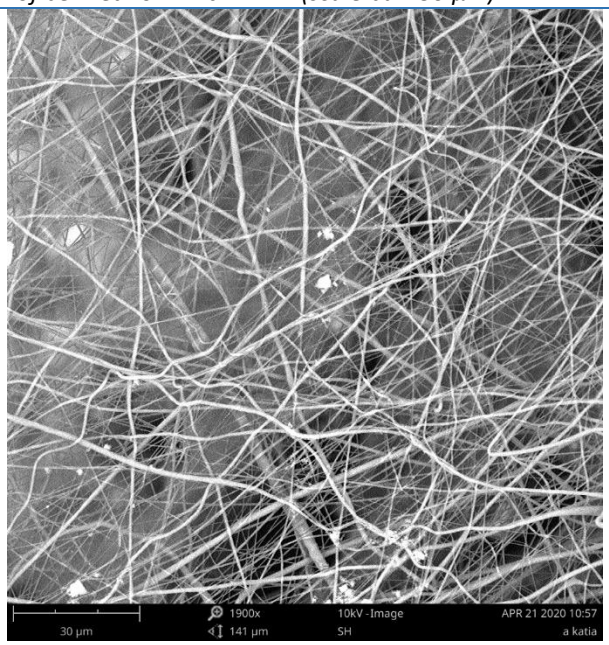

*Fig. 6. SEM image of the nanofiber network **without** PVP-I (scale bar: 30 µm).*

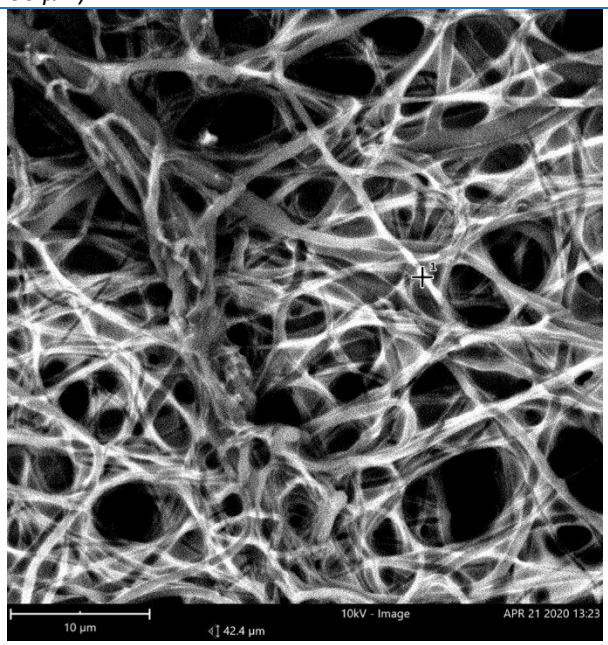

*Fig. 7. SEM image of the nanofiber network **without** PVP-I (scale bar: 10 µm).*

As could be seen from Fig. 4, Fig. 6 and Fig. 7, the addition of PVP-I not only confers effective antiviral properties, but also enables smaller pore-network that allows free gas transfer whole keeping nano-size particles out.

The effectivity of the MAYA Sticker is even improved under 'heavy duty'; i.e., due to the unique 3D structure, the porosity is reduced, meaning that the ability of microorganisms, including infectious viruses, to penetrate vis the MAYA Sticker is dramatically reduced. Fig. 8 and Fig. 9 represent the porosity of the dry sticker in comparison to wet sticker, respectively.

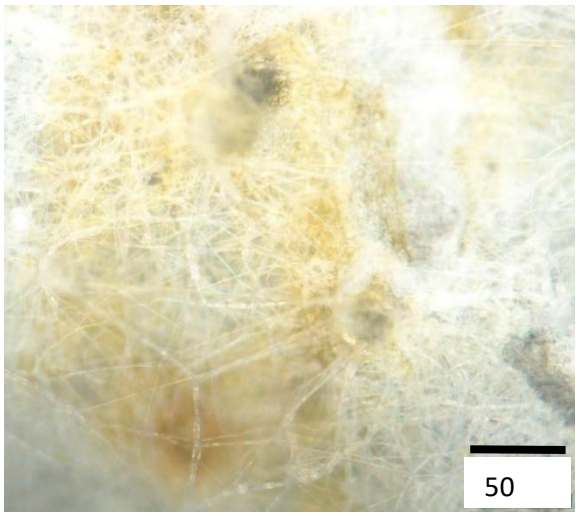

Fig. 8. Optical microscope image of the dry sticker fiber network (scale bar: 50 µm).

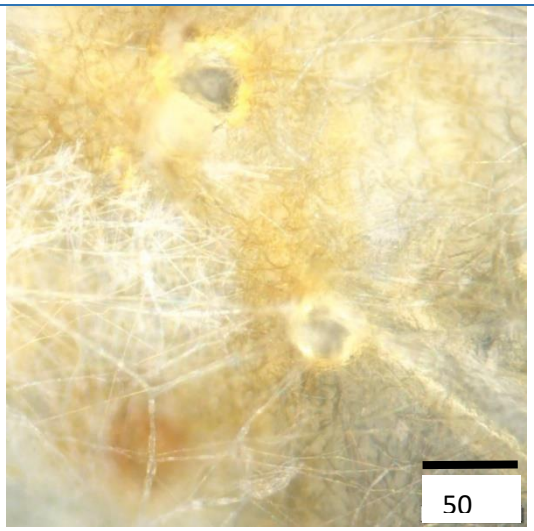

Fig. 9. Optical microscope image of the wet (water) sticker fiber network (scale bar: 50 µm).

Table 1 describes the weight-concentration of the 3 elements, carbon, oxygen and iodine, total 99.23%.

Table 1. Energy-dispersive X-ray (EDX) analysis with scanning electron microscopes (SEM) for weight-concentration of carbon, oxygen and iodine. FOV (field of view): 42.4 µm, Mode: 10kV - Image, Detector: BSD (back-scattered electron detector) Full.

Element №	Element symbol	Element name	Atomic conc.	Weight conc.
6	C	Carbon	65.78	62.20
8	O	Oxygen	17.05	23.80
53	I	Iodine	1.00	13.23
			Total	**99.23**

2. Inactivation of *Coccolithoviruses* as a model system

The purpose of this study was to examine the efficacy of the MAYA Sticker for inactivation of viruses.

Coccolithoviruses (*Phycodnaviridae*), EhV201, infect and lyse the most ubiquitous and successful coccolithophorid in modern oceans, *Emiliania huxleyi*. So far, the genomes of 13 of these giant lytic viruses (i.e., *Emiliania huxleyi* viruses—EhVs) have been sequenced, assembled, and annotated. Thus, Coccolithoviruses serve as a good nonvirulent model for *in vitro* activation and inactivation.

To quantify the potential of the fiber mats to inactivate the virus, a most probable number (MPN) experiment was conducted; i.e., getting quantitative data on concentrations of discrete items from positive/negative (incidence) data.

Table 2 and Fig. 10 below display the viral activity of the tested samples. For the untreated PCL mask (1), only a slight decrease in viral activity was observed compared to the control group "virus."

The addition of povidone-iodine to PCL nanofiber mats led to a complete reduction of the viral activity with no measurable active viral particles. Table 2 summarizes the obtained data.

Table 2: Viral activity after contact with fiber mats in comparison to control group (Virus).

	MPN	Log_{10} MPN	SD Log_{10} MPN
Virus (control)	3.4E+07	7.5	0.17
Virus on PCL mask	1.0E+07	7.0	0.17
Virus on PCL mask +20% PVP-I	0		
Virus on PCL mask +70% PVP-I	0		

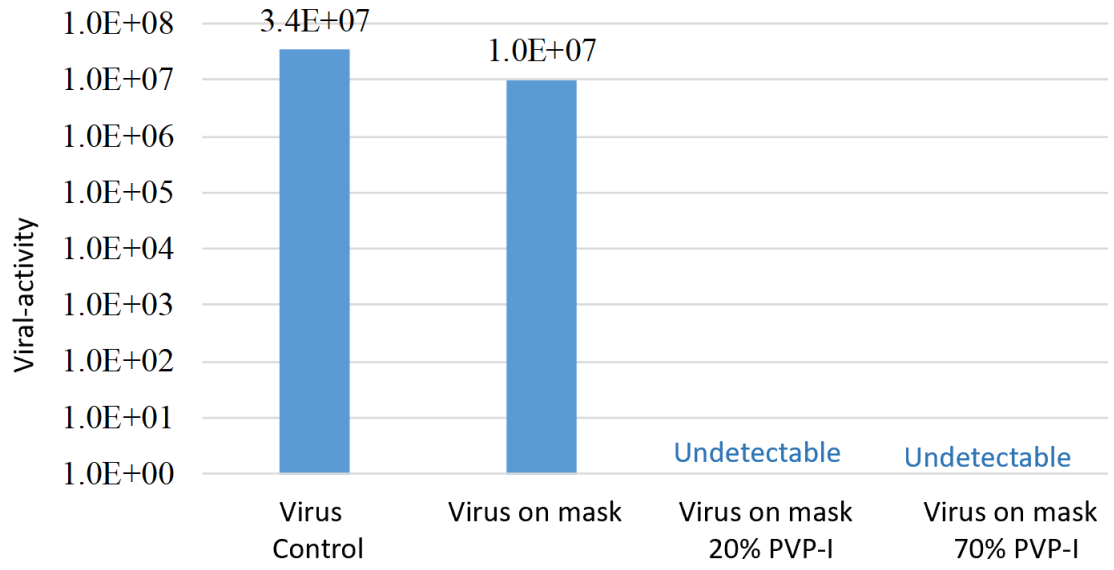

Fig. 10. Viral activity after contact with fiber mats in comparison to control group "Virus".

Conclusions: Comparing to the control group (virus, free virus not on a mask), in untreated polycaprolactone (PCL) mask, only a slight decrease in viral activity was observed.

The addition of povidone-iodine (PVP-I) to the PCL nanofiber mats led to a complete reduction of the viral activity with no measurable active viral units.

3. Survival of human HCoV-229E coronavirus following disinfection using the MAYA Stickers

The purpose of this study was to determine the infective amount of the HCoV-229E coronavirus remaining after disinfection using the MAYA Sticker.

MRC-5 (Medical Research Council cell strain 5) cells were used, a diploid human cell culture line composed of fibroblasts, originally developed from research deriving lung tissue of a 14-week-old aborted Caucasian male fetus.

Real-time-PCR analyses were performed to estimate the virus replicates duplicated in the cells.

The MAYA Stickers were tested with 3 different concentration of PVP-I: A – 0.01 mg/cm^2, B – 0.06 mg/cm^2, and C – 0.4 mg/cm^2.

Results are detailed in the following Fig. 11 and Table 3.

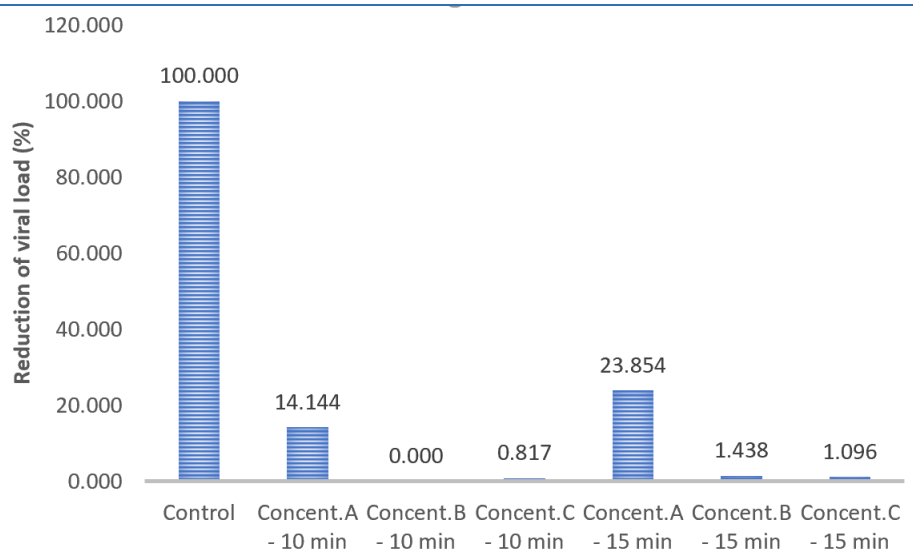

Fig. 11. Reduction of viral load (%) following administration of the MAYA Sticker soaked with various concentration of PVP-I.

Table 3: Percentage do survived viruses after treatments.

Treatment	% of survived viruses	№ of virus replica after treatment
Control (no treatment)	100.000	1.77E+08
Concent.A - 10 min	14.144	25058367
Concent.B - 10 min	0.000	27
Concent.C - 10 min	0.817	1446762
Concent.A - 15 min	23.854	42260400
Concent.B - 15 min	1.438	2547864
Concent.C - 15 min	1.096	1941534

Conclusions: The MAYA Sticker reduced the viral load by 78.2% (concentration A (0.01 mg/cm^2), 15 minutes) to >98% (concentrations B (0.06 mg/cm^2) and C (0.4 mg/cm^2), 10 and 15 minutes) comparing to the control group (no reduction in viral load).

4. Optimization of the ergonomic design

The adaptation of the MAYA Sticker to the use of medical teams was tested in several health centers in Israel; Galilee Medical Center in Nahariya, Bnai Zion Medical Center in Haifa, Ziv Medical Center in Safed, Tel Aviv Sourasky Medical Center (Ichilov) in Tel Aviv, Sheba Medical Center in Tel HaShomer, Sha'arei Zedek in Jerusalem and Rambam Health Care Campus in Haifa.

The trial was performed to collect feedback from the teams, using a dedicated application developed for this purpose.

The data collection and analysis were carried out by a joint team led by the Galilee Medical Center.

The feedback received during the stickers' development was of greatly assistance and helped to determine the ergonomic factors.

Results are detailed in the following Fig. 12 and Fig. 13.

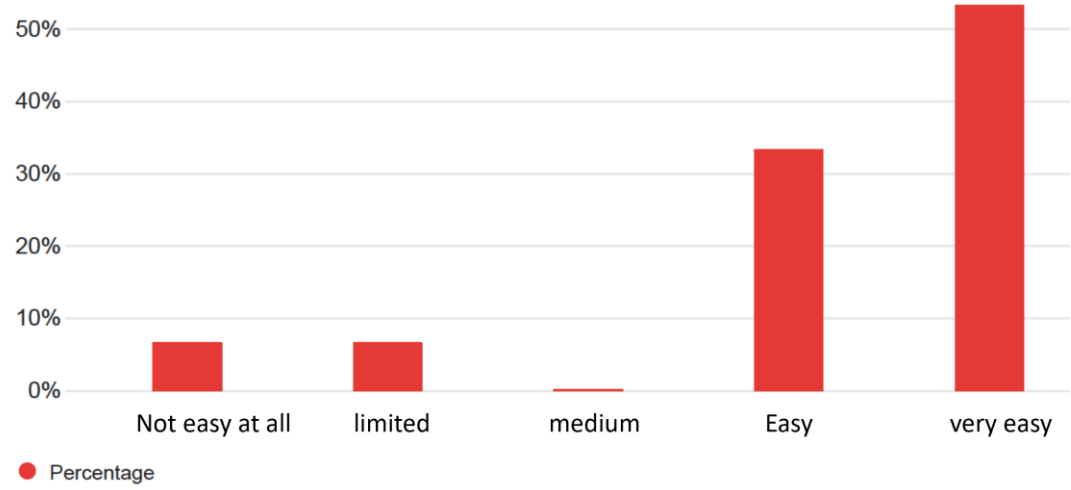

Fig. 12. Distribution of the answers to the question: "Is it easy to stick the MAYA on surgical mask?"

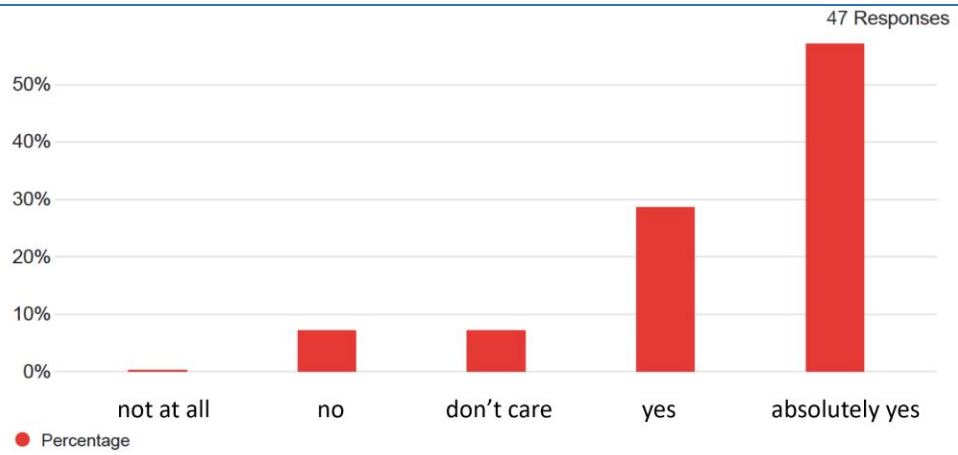

Fig. 13. Distribution of the answers to the question: "If you have to use a surgical mask, do you feel safer with the MAYA Sticker?"

Conclusions: As illustrated in Fig. 12, >87% of the healthcare team members found the MAYA Sticker as easy to stick on the surgical mask.

As could be seen from Fig. 13, >80% of the healthcare team members indicated that they feel safer with the MAYA Sticker.

5. Human clinical trial: upgrading surgical mask effectiveness against the SARS-CoV-2 with an antiviral nanofiber sticker[4].

The clinical trial was performed in Galilee Medical Center, Nahariya, Israel (Oral and Maxillofacial Department, Infectious Diseases Department, Geriatric Department and Department of Otolaryngology - Head and Neck Surgery) and The Azrieli Faculty of Medicine, Bar-Ilan University in Ramat Gan and Safed, Israel, headed by the NanoEngineering Group, Faculty of Mechanical Engineering, Technion-Israel Institute of Technology, Haifa, Israel.

Background

Recent studies have indicated that aerosol and fomite transmission of SARS-CoV-2 is possible, since the virus can remain effective in respiratory droplets for hours. While facemasks have been

[4] Samer Srouji, Amiel A. Dror, Kaykov Edward, Mona Shehadeh, Yael Ziv, Yuval Eshed, Massad Barhoum and Eyal Zussman (2020). Upgrading Surgical Mask Effectiveness against the SARS-CoV-2 with an Antiviral Nanofiber Sticker. Submitted to the New England Journal of Medicine.

advocated as a standard means of protection, particles in the range of 0.04-0.2 µm have been shown to penetrate surgical masks. With an average size falling within this range (0.12 µm)[5], it was not surprising that a recent study detected SARS-CoV-2 (NL63, OC43, HKU1, and 229E) on the outer surface of surgical masks used by SARS-CoV-2-affected individuals[6]. Thus, the effectiveness of facemask protection in the prevention of viral spread is still under debate during the current ongoing global SARS-CoV-2 pandemic[7].

Objective

To upgrade the performance of standard surgical masks by applying an innovative anti-viral protection sticker.

Methods and Findings

The single-use innovative MAYA Sticker is composed of a nonwoven polymer nanofibers filter coated with a biocidal agent, and is affixed to the outer surface of the mask. The nanofibers are comprised of polycaprolactone, a biocompatible material. The filter density and porosity are circa 93% and 0.1 g/cm^3, respectively. Nanofibers are coated with 0.5 mg/cm^2 povidone-iodine (PVP-I), a biocidal agent homogeneously dispersed and coating the nanofiber fabric.

To test the efficacy of the anti-viral MAYA Sticker in reducing SARS-CoV-2 spread, a controlled comparative surgical mask contamination study in six patients positively diagnosed (RT-PCR) with SARS-CoV- 2 less than 72 hours prior to mask testing.

The clinical presenting symptoms included fever, shortness of breath, cough, and myalgia.

The study was conducted in airborne infection isolation rooms in the dedicated COVID-19 department at the Galilee Medical Center, Israel. The rooms had an average temperature of 23°C, with a relative humidity of 55% – 60%. Patients wore the surgical mask (Halyard, The Lite One) for 1 h, and thereafter a surgical mask with the anti-viral MAYA Sticker attached to the outer surface of the mask for 1 h.

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5 Lee SA, Grinshpun SA, Reponen T. Respiratory performance offered by N95 respirators and surgical masks: Human subject evaluation with NaCl aerosol representing bacterial and viral particle size range. Ann Occup Hyg 2008.

6 Leung NHL, Chu DKW, Shiu EYC, *et al.* Respiratory virus shedding in exhaled breath and efficacy of face masks. Nat Med 2020.

7 van Doremalen N, Bushmaker T, Morris DH, et al. Aerosol and Surface Stability of SARS-CoV-2 as Compared with SARS-CoV-1. N Engl J Med 2020.

Addition of the MAYA Sticker to the mask did not affect patient exhalation patterns, breathing efforts, or vital signs. All participants coughed at least 5 times during the 1 h exhaled breath collection.

The outer surfaces of the mask and the outer surface of the anti-viral MAYA Stickers were swabbed after the 1 h usage with aseptic Dacron swabs.

All swabs were then immediately transferred to an in-house biosafety level-3 laboratory and immediately processed. A commercial real-time RT-PCR kit (BGI, Shenzhen, China) was used to detect SARS-CoV-2 in the samples, as per the manufacturer's protocol. A sigmoidal amplification curve and threshold cycle (Ct value) <38 indicated a positive sample.

Four out of six outer surgical mask surface samples contained SARS-CoV-2 virions, whereas all swabs from the outer surface of the MAYA Sticker were free of SARS-CoV-2 viruses, as indicated in Table 4.

Table 4. Patient characteristics

Characteristics	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5	Patient 6
Age (yrs)	67	48	70	45	84	59
Sex	F	M	M	F	F	N
Symptoms at presentation	fever, shortness of breath, cough, myalgia	fever, shortness of breath, myalgia	fever, shortness of breath, cough	fever, shortness of breath, myalgia	fever, shortness of breath, cough	fever, shortness of breath, cough
Diagnosis	Pneumonia	Upper respiratory infection	Pneumonia	Upper respiratory infection	Upper respiratory infection	Upper respiratory infection
Day of hospitalization at testing	3	6	2	1	2	4
Viral load on surgical mask without sticker (RT-PCR cycle)	ND	ND	D	D	D	D
Viral load on surgical mask with sticker (RT-PCR cycle) ND	ND	ND	ND	ND	ND	ND
ND = not detected; D = detected; M = male; F = female; SARS-COV-2 = Severe acute respiratory syndrome coronavirus 2; A sigmoidal amplification curve and a threshold cycle (Ct value) <38 was determined to indicate a positive sample.						

Discussion

Standard surgical masks have long been in use to reduce the load of viral transmission; however, their protection against SARS-CoV-2 remains questionable.

The data presented in this study support previous reports of transmission of virus-loaded aerosols through surgical masks, as detected by swabs sampling of the outer surface of the mask[8].

While masks efficacy is traditionally enhanced by reducing the mesh porosity, applying this approach to block the penetration of the SARS-Cov-2 would result in very low mask permeability, subsequently making breathing difficult. This proposed anti-viral MAYA Sticker attached to the outer surface of the surgical mask fully inhibited viral survival on the outer surface of the mask. When a droplet containing viruses hits the anti-viral MAYA Sticker, the droplet is absorbed into the nanofiber fabric, where viruses become trapped between the nanofibers, and inactivated by the PVP-1 biocidal component. As a well-known biocidal, it was recently shown that 1% PVP-I inhibits SARS-COV-2 on surfaces within 30 sec[9]. The high surface area of the nanofibers within the antiviral MAYA Sticker and the typical size of the adsorbed droplet dictates an approximate effective concentration of 10% PVP-I, assumed to inactivate SARS-CoV-2 in a matter of seconds.

Additional unpublished data from parallel experiments showed that contamination of anti-viral MAYA Stickers with a droplet of concentrated coronaviruses (229E) led to 99% inactivation following 10 minutes.

Conclusions

Upgrading surgical masks with anti-viral MAYA Stickers has the potential to eliminate the spread of infection by affected individuals donning the mask, and to similarly protect the healthy population against SARS-CoV-2 infection.

The MAYA innovative anti-viral facemask sticker synergizes between principles of nanofiber physical filtration and active biological filtration, which can be applied in the future for antiviral, antimicrobial, and antifungal applications.

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8 Bae S, Kim M-C, Kim JY, et al. Effectiveness of Surgical and Cotton Masks in Blocking SARS-CoV-2: A Controlled Comparison in 4 Patients. Ann Intern Med 2020.

9 Kampf G, Todt D, Pfaender S, Steinmann E. Persistence of coronaviruses on inanimate surfaces and their inactivation with biocidal agents. J. Hosp. Infect. 2020.