A COMPACT AND WIRELESS LUNG FUNCTION TEST DEVICE FOR VETERINARY MEDICINE

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ABSTRACT

The clinical evaluation of respiratory mechanics in horses is nowadays based on invasive methods that may require sedation. The forced oscillation technique (FOT), known also as oscillometry, is a non-invasive method for lung function testing used in humans that doesn't require subject collaboration. Current FOT devices suitable to be used on horses are complex, cumbersome, expensive, and difficult to be applied in quine veterinary settings. This thesis aims to develop a small, cheap, portable and easy-to-use FOT device according to a novel approach in which the pressure waveforms are generated by a fan moved by the rotational speed of a brushless DC motor. This new approach has been recently demonstrated by a proof-of-concept device. From results of this concept, the detailed specifications of a device for clinical use was defined and both the device and a software application for wireless operations and control were designed and developed. This device was validated in vitro, providing an average error of $0.0789\ cmH_2O \cdot {}^{s}/_{L}$ and $0.2433\ cmH_2O \cdot {}^{s}/_{L}$, respectively, in measuring R and X. The device was also tested in-vivo on five healthy horses and a horse diagnosed with SEA (Severe Equine Asthma), demonstrating good tolerability of the procedure, correct functioning of the device, and reliability in resistance and reactance of horses' respiratory system estimation. This novel approach for applying FOT allowed the development of a compact, wireless, inexpensive, and portable device for the non-invasive evaluation of respiratory mechanics in spontaneously breathing horses, providing a valuable new tool for improving veterinary respiratory medicine.

I. INTRODUCTION

Equine asthma (SEA) is associated with lower airway inflammation and obstruction and is horses' most frequent respiratory condition. Up to 80% of horses will be affected by SEA at least one time in their life, causing several deficits during physical exercise.

Recurrent airway obstruction (RAO), or heaves, previously known as Chronic Obstructive pulmonary disease COPD [1], refers to diseases that cause airflow blockage and breathing-related problems. The pathology can involve different clinical signs, such as small airway obstruction, inflammation, bronchospasm, excessive mucus, and thickening of the airway wall [1].

RAO diagnosis involves the analysis of the clinical history of the horse and physical examination. Pulmonary Function Tests (PFT) objectively evaluate the lung and airway conditions. The main disadvantage of these methods is linked to the wide range of physiologically acceptable values, requiring highly specialized expertise to diagnose RAO early. Furthermore, such tests might be based on invasive procedures that may require sedation of the animal [2]. Finally, even the most widely used techniques are not sufficiently sensitive alone, so the diagnosis is largely based on the animal's clinical history.

An alternative approach, recently proposed by the TechRes Lab of the Politecnico di Milano University, is based on the estimation of the mechanical properties of the horse's respiratory system by means of the Forced Oscillation Technique (FOT).

Forced Oscillation Technique

The Forced Oscillation Technique was introduced by Dubois et al. in 1956. It consists in superimposing a small-amplitude, high-frequency signal to the spontaneous breathing

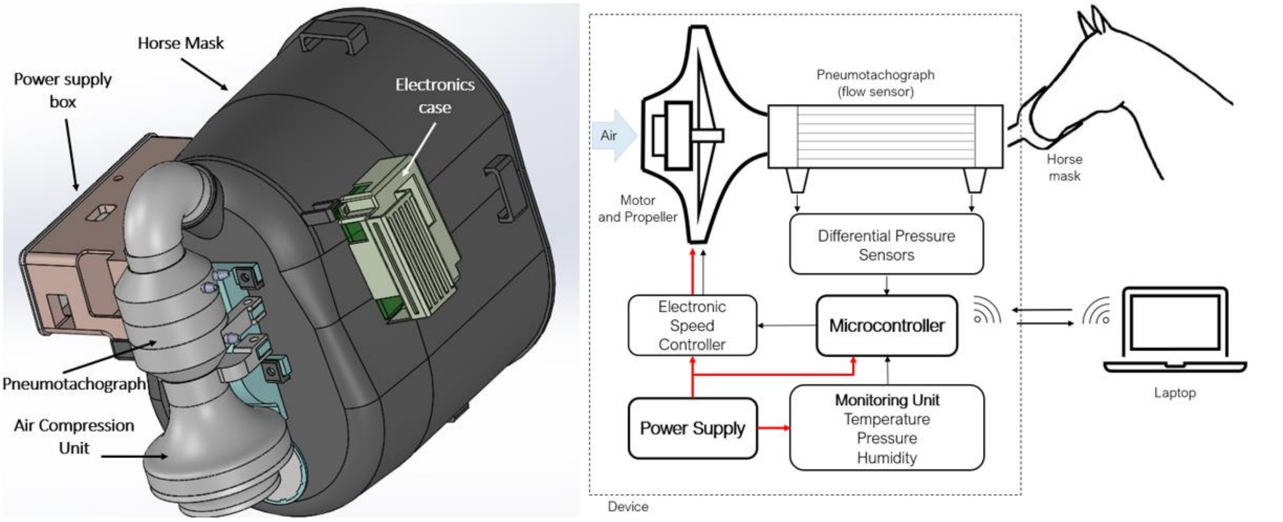

Figure A Left: mechanical design of the device mounted on the custom 3D printed mask.. Right: schematic architecture of the device.

activity of the subject under test. The complex ratio of the pressure and flow measured at the airway opening provides the so-called "impedance" of the respiratory system. The impedance is a complex number made of a Real part, the resistance, representative of the resistive properties of the lung, and an Imaginary component, the reactance, that depends on the inertial and elastic properties of the measured system.

FOT does not require the collaboration of the patient since it is based on non-invasive measurements on normal breathing subjects, being an ideal technique for animal applications.

In 1989 Young and Hall performed tests on ponies with a specifically modified FOT setup using stimulation frequencies from 3 Hz to 40 Hz [3].

Further studies by Young and Tesarowski were later conducted on adult horses, first free from clinical signs of respiratory diseases, then also in horses with reversible allergic airway disease. From the results of this study Young and Tesarowski concluded that the equine impedance-frequency curve may be similar to that of humans but shifted down in frequency because of the larger mass of the horse [4].

A new approach

The forced oscillation technique (FOT) allows the non-invasive assessment of respiratory mechanics during spontaneous breathing; however, current devices are complex, cumbersome, expensive, and difficult to be applied to horses.

Recently, a new approach for FOT measurements has been proposed and tested on healthy and asthmatic horses by the TechRes Lab of the Politecnico di Milano [2]. The innovative method employs a microcontroller-based device that uses a ducted fan to generate the pressure oscillations at the airways opening of the animal. This project aims at improving the design of the previously developed prototype. The improved version will integrate all the necessary components in a custom face mask while wirelessly transmitting the data to a specifically designed Graphical User Interface.

II. MATERIALS AND METHODS

The device has been developed according to some pivotal points. In particular, the device has to:

- Superimpose pressure oscillations with adjustable amplitude and stimulation frequency from 1 Hz to 7 Hz to the normal breathing of the animal.
- Correctly measure pressure and flow at the airways opening of the animal.
- Enhance portability by using wireless communication with the host machine and by developing a cross-platform application

for measurement control and data processing.

- Be solid and sturdy to work even after abrupt movements of the animal, enhancing a modular structure in order to change the components if required quickly.

System Architecture

The system is composed of different components which can be grouped as functional blocks.

The main component is the air compression unit, composed of a brushless DC motor (EMAX LS2207-2550KV) driven by an Electronic Speed Controller (ESC) coupled with a suitable propeller, which is responsible for pressure and flow generation.

A differential pressure sensor (ELVR-L10D) measures pressure information at the subject airways opening, while another sensor (ELVR-L01D) is used to acquire information about pressure drop over the resistance of a custom-made pneumotachograph used to measure the air flow. In order to control the delivery of the pressure oscillating pattern to be superimposed on the subject's spontaneous breath, a microcontroller implements a closed-loop control to regulate the motor speed through an electronic speed controller (ESC).

A monitoring unit composed of a temperature and humidity sensor (HIH6130/6131) and an absolute pressure sensor (MS5637-02BA03) provides information about environmental parameters so that collected data can be compensated for environmental variations.

The whole system is embedded into a 3D-printed modular structure that composes the horse mask. The mask also hosts a silicone seal and a three-cell, 12 V LiPo battery, which provides the power supply for the hardware. A scheme of the system architecture is reported in Figure A.

Firmware - Control Unit

The core of the system is the microcontroller (Espressif ESP32 microcontroller), which is responsible for the low-level control of the device and the wireless data transmission between the system and the user's laptop.

The firmware was developed to ensure that the device performs a complete measurement autonomously.

The system works at a positive pressure, which is necessary to generate pressure oscillation by varying motor speed around a stable value, without changing rotation direction, requiring too much energy. Control is managed by PID controllers responsible for reaching and maintaining the pressure offset (~ 3 cmH2O), delivering a constant amplitude (1 cmH2O) sinusoidal pressure wave superimposed to the horse breathing pattern and compensating average pressure changing at subject airways opening during spontaneous breathing.

The microcontroller embeds a wireless module, which allows for Wi-Fi connection and wireless data transmission. TCP protocol allows to establish a reliable connection between the two devices connected to the same Local Area Network (LAN). A custom communication protocol allows the two machines to exchange data.

Software – User Interface

An intuitive user interface ensures the correct device usage and performs data processing required to evaluate mechanical properties. A cross-platform desktop application was developed using Electron js framework for this scope.

The application is responsible for user-device interaction managing laptop-microcontroller data exchange depending on user actions.

When the measure ends, pressure and flow signals are filtered with a digital bandpass 2nd order Butterworth filter with a cut-off band of FOT Frequency ±0.5 Hz. Impedance computation starts from filtered pressure and flow signals and exploits a least-square algorithm. Resistance is obtained considering the real part of the computed impedance, while reactance consists of the imaginary part.

Due to the subject spontaneous breathing, both resistance and reactance signals are subjected to abrupt changes in correspondence to the end of inspiration and expiration. For this reason, the flow signal is filtered and integrated to obtain a volume trace form which breathing phases are determined considering the volume's local

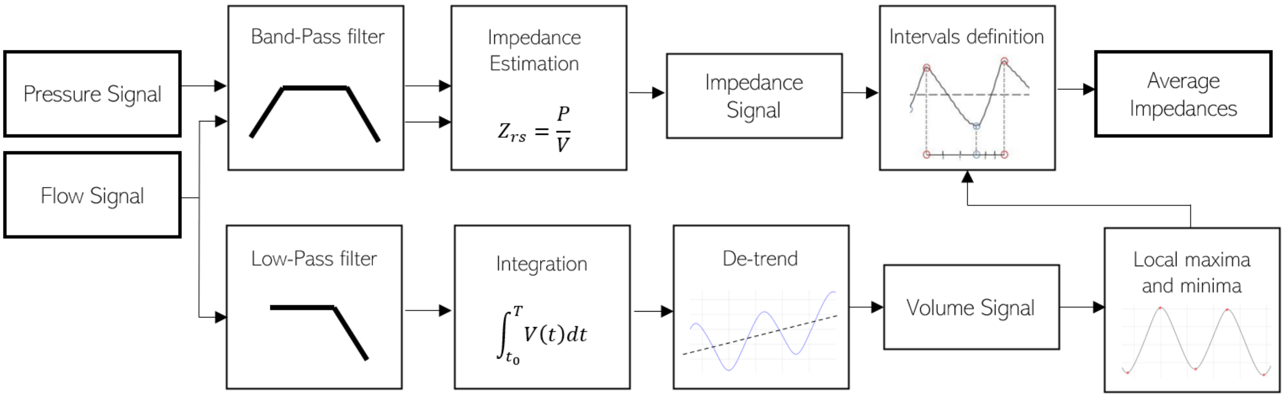

Figure B – Data processing algorithm. While both pressure and flow signals are band-passed before impedance estimation, tidal volume trace is extrapolated from a low-passed flow trace. Volume maxima and minima location constitute time of End of Inspiration (EoI) and End of Expiration (EoE) respectively. From this information it's possible to compute average impedances during inspiratory and expiratory breathing phases.

maxima and minima. Each breathing phase is divided into three equal time intervals; impedance is computed as the average of the values corresponding to the central intervals for each breathing phase. A scheme reporting the algorithm steps is depicted in Figure B.

In-vitro validation protocol

Experimental Setup

The device was firstly validated in-vitro to evaluate its performance. During the tests, the device was connected to a custom-built test lung made of a glass carboy of 55.75 L, used to simulate the compliance of the respiratory system, connected to a flow resistor containing 28 capillary tubes in parallel each 15 cm long with an internal diameter of 2 mm to simulate the resistance and inertance. The theoretical values of the mechanical parameters of the model were computed according to the model proposed by Franken et al. [5]. The resulting setup has a resistance of 2.57 $cmH_2O \cdot s/L$, compliance of 0.04 L/cmH_2O, and inertance of 0.0274 $cmH_2O \cdot s^2/L$.

Sine Generation

The quality of the sinusoidal waveform was assessed by comparing the recorded pressure and flow measurements with an ideal sinusoid. The so-called Pressure Shape Index (PSI) and Flow Shape Index (FSI) can be computed for each point of the recording, considering a window of N samples covering an entire period of the sinusoid, as:

$$SI = \frac{\sum_i^N |(a_0 \cos(x_i) + b_0 \sin(x_i)) - recorded\ signal_i|}{\sum_i^N |recorded\ signal_i|}$$

Moreover, for each stimulation frequency, it is possible to compute the power spectrum to analyze the frequency content of the pressure oscillations generated by the device. The Fourier power spectrum, the PSI, and the FSI were computed for every measurement. The Fourier power spectrum was calculated for each frequency, from 0 to 125 Hz, with a sampling frequency of 250 Hz.

Impedance estimation

The accuracy of the impedance estimation was assessed by connecting the device to the test lung while delivering different FOT frequencies, from 1 to 7 Hz, with 1 Hz resolution. The testing time for each frequency was set to 15 s and the peak-to-peak amplitude of the pressure oscillations was set to 0.75 cmH_2O.

In-Vivo Validation protocol

The in-vivo acquisitions were performed at the faculty of veterinary medicine of Università degli Studi di Milano, Lodi. Tests were performed to understand whether the procedure of measure is feasible and to evaluate the quality of measured impedance by comparing collected data with the veterinary assessment of horses' conditions. A further scope was the qualitative evaluation of the difference in measured respiratory impedances between healthy horses and asthmatic ones.

The study population is composed of 6 horses: five healthy horses and one diagnosed with Severe Equine Asthma (SEA). The acquisition protocol consists of FOT recording over a range of frequencies from 1 Hz to 7 Hz with a step of 1 Hz for 30 seconds each. Pressure oscillations were characterized by a peak-to-peak amplitude of 1 cmH_2O superimposed to a positive pressure of 3 cmH_20. Measurements were repeated three times on each subject.

III - RESULTS

In-vitro validation

The quality assessment of the sinusoidal pressure and flow waveform computed by means of PSI and FSI showed results in line with the International FOT Guidelines. For every frequency, the PSI and FSI values were below the threshold of 0.1, which indicates the quality of the sinusoidal waveforms is comparable to commercially available devices for human FOT.

PSDs for pressure traces are reported in Figure C, enhancing the peaks at each FOT frequency. As it can be seen, the frequency content of the pressure signal has a peak in correspondence to the stimulation frequency that is ~40 dB over the other frequencies.

Table 1 reports the impedance measurement of the test lung for each frequency. The average errors for both R and X are 0.0789 $cmH_2O \cdot {}^{s}/_{L}$ and 0.2433 $cmH_2O \cdot {}^{s}/_{L}$ respectively.

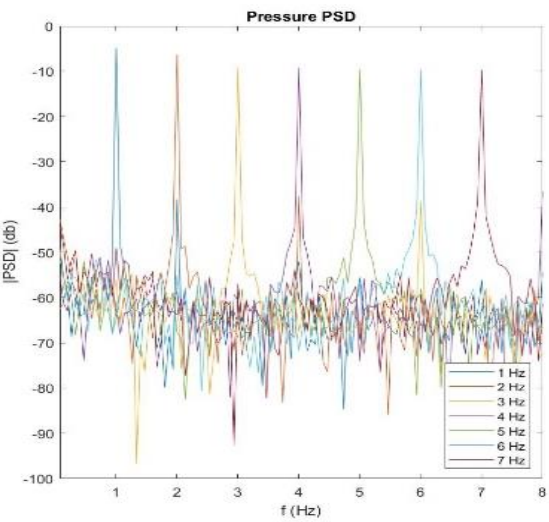

Figure C – Pressure PSD at different FOT frequency.

Table 1 - Resistance and reactance values. FOT estimate vs theoretical model.

frequency	R_{FOT}	R_{MODEL}	X_{FOT}	X_{MODEL}
1 Hz	2.74	2.58	-4.096	-3.984
2 Hz	2.57	2.56	-1.85	-1.736
3 Hz	2.56	2.56	-1.036	-0.870
4 Hz	2.59	2.56	-0.592	-0.350
5 Hz	2.62	2.56	-0.252	0.029
6 Hz	2.69	2.57	-0.020	0.341
7 Hz	2.74	2.57	0.193	0.612

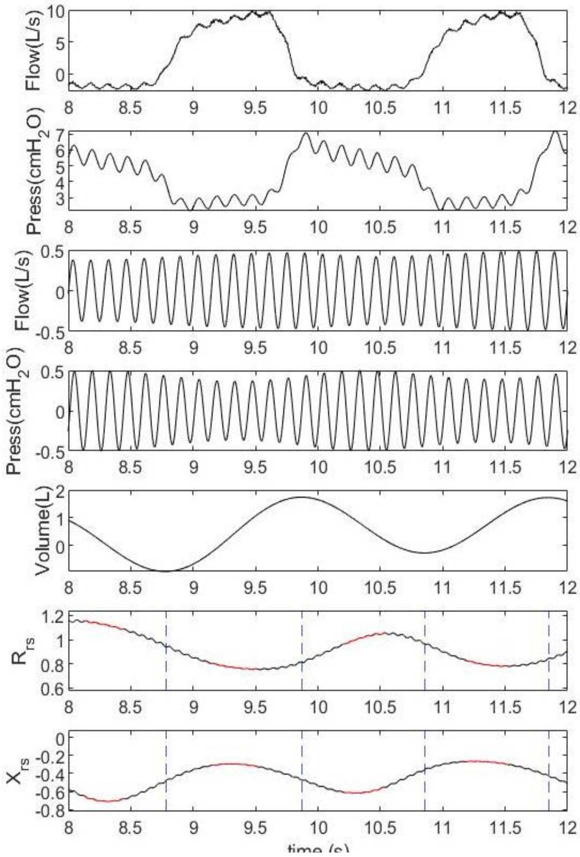

Figure D - From top to bottom: raw flow and pressure traces. Band-passed flow and pressure traces. Volume trace and indication of maxima and minima. Resistance and reactance traces. Red sections are referred to the second third of each respiratory phases and are used for average computation.

In-vivo validation

Impedance parameters were extracted using the automatic offline algorithm in the software application. Resistance and reactance are computed started from filtered pressure and flow signals in correspondence to the central section of both expiratory and inspiratory phases. Figure D reports examples of traces from the processing algorithm.

Resistance and reactance traces were computed for both the expiratory and inspiratory phases. Measurements were repeated three times among different days for each horse. Figure E shows the resistance and the reactance of the measurements on the six horses, expressed as mean (SD). Mean values are represented as circles, while standard deviation is represented as a square on one side of the curve.

Moreover, by analysing the expiratory and inspiratory reactance separately, it is possible to compute the ΔXrs, that has been shown in humans to be an indicator of Expiratory Flow Limitation (EFL) in COPD patients. There is no difference between the inspiratory and expiratory reactance of healthy horses (ΔXrs ~ 0 for each frequency). In contrast, the asthmatic horse showed a higher ΔXrs, agreeing with EFL associated with human COPD and SEA in horses.

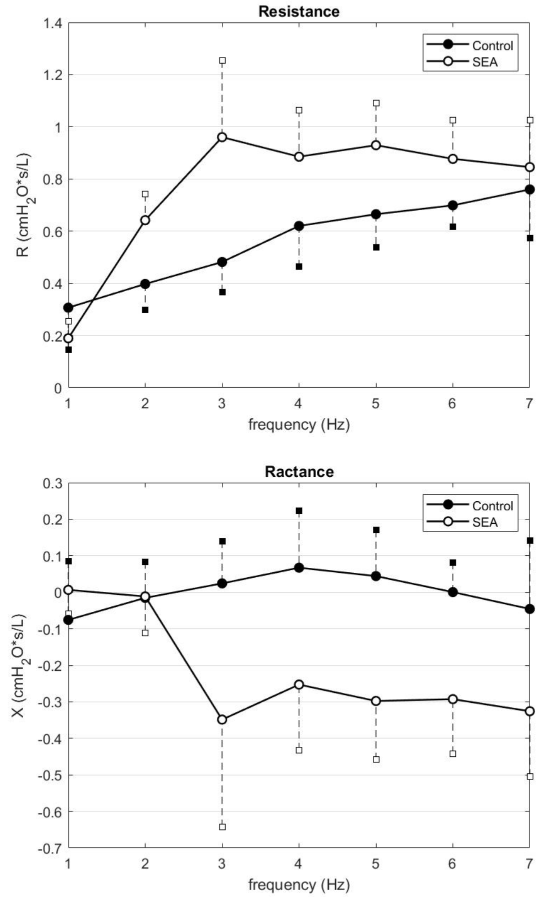

Figure E – Resistance (top) and Reactance (bottom) values for control group and asthmatic one. Mean and standard deviation are reported.

IV – Discussion

Equine asthma is a debilitating pathology that occurs in 80% of horses at least one time. Given the impact of such disorders on horses' physical performances, it is crucial to have access to early diagnosis systems that could be used for preventive treatment strategies. Because of the lack of similar commercially available devices, this thesis work aimed to design and realize a portable device for performing Forced Oscillation Technique tests on horses to assess lung mechanics in a non-invasive and objective way.

The device was developed and in-vitro validated at the TechRes Lab of Politecnico di Milano. The in-vitro tests demonstrated the possibility of transmitting and receiving data exploiting a Wi-Fi communication between the device and a specifically designed Graphical User Interface. Moreover, the mechanical tests showed good agreements between the mechanical properties of a test lung estimated using the device and the theoretical ones.

All the electronics, power supply, and necessary instrumentation have been designed to be fitted on a 3D printed mask that resembles the horse's face. The entire horse mask, air compression unit, and pneumotach were designed to constitute a solid, compact structure. The electronic PCB was designed to host all the necessary components minimizing area usage. The entire system is powered by a Lithium-Polymer battery, which can be easily removed from its case to be changed or charged. Wireless technology and portable power supply allow the device to be used in a context different from the ordinary medical room.

The portability and easiness of use of the developed device allowed a first batch of in-vivo measurements that consented to evaluate its performances in the field of application.

In-vivo validation confirmed the feasibility of the procedure, showing that pressure oscillation doesn't interfere with horses' spontaneous breathing. Mechanical properties were correctly assessed in 6 horses, showing the possibility to obtain a reliable measure with a non-invasive, fast, and simple procedure. The possibility to distinguish between healthy and impaired horses was explored, confirming the feasibility of the assessment.

Innovation of this work relies on the non-invasiveness and simplicity of the technique, allowing to perform tests in a non-controlled environment, which is fundamental for this application. Furthermore, the graphic user interface developed helps the clinician during the acquisition, extending the possibility also to a non-highly trained specialist to handle the test. These two characteristics of the device may allow wide use to monitor horses' lung mechanics, helping the clinician perform faster and more accurate and objective diagnoses.

Even if the number of asthmatic horses is limited, it is possible to appreciate a difference in resistance and reactance values between healthy and asthmatic horses. The results agree with findings in the literature; the shift in resistance is upward and more accentuated at lower frequencies, caused by an increased central airways resistance due to the presence of mucus within the airways. On the other hand, the reactance of the asthmatic horse decreases at mid frequencies compared to healthy horses due to the obstructive pathophysiology of asthma.

V – Conclusions

The novel approach for applying FOT allowed the development of a small, affordable, and portable device for the non-invasive evaluation of respiratory mechanics in spontaneously breathing horses. The device proved to be well-tolerated by horses and easy to operate, providing a useful new tool for improving veterinary respiratory medicine.

Even though the population of horses used for the in-vivo validation was small and only one asthmatic horse was included, the results confirmed the feasibility of extracting meaningful mechanical parameters using the developed device in an in-vivo context.

The device will be employed in a clinical study collaborating with the University of Montreal (Canada) and the Università Degli Studi di Milano. The protocol includes measurements on an extended sample of animals, which accounts for a large horse's variability, including more asthmatic animals and a cohort of asymptomatic subjects.

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