Experimental analysis of particles flow inside the Volumatic® spacer

J. P. M. Costa[1], J. C. F. Teixeira[1], L. F. Silva[1]
& S. F. C. T. Teixeira[2]
[1]*Department of Mechanical Engineering, School of Engineering, University of Minho, Portugal*
[2]Department of Production and Systems, *School of Engineering,* University *of Minho, Portugal*

Abstract

At present there are several studies regarding the performance of many pressurized metered-dose inhalers (pMDIs), more precisely, spacers with special emphasis on the study and analysis of the fluids using (Computational Fluids Dynamics (CFD) software, in this specific case, Fluent™. The Volumatic® is the most commonly used spacer nowadays, and, therefore, the one that has been studied more. However, and in spite of all the simulations carried out with air and drug particles, there is no confirmation with an actual experimental testing procedure regarding the drug dynamics inside a particular spacer. Therefore, and to validate the simulated studies carried out before in this area, a mechanical system able to duplicate the respiratory system was designed and implemented so that the same conditions inputted to the simulation tools could be tested and compared. In order to collect the data for this analysis, the Laser Doppler Anemometry (LDA) technique was used, which enables the measurement of the velocity of the particles through the center and some frontier regions of the studied spacer. As expected, it was possible to observe areas of recirculation, with a similar tendency to those obtained during simulation. The main difference relied on the absolute values of the velocity, which might be related to the lack of symmetry along the spacer and also probably due to the turbulent flow that probably exists inside the tube included in the mechanism used to simulate the respiratory system.
Keywords: spacers, pMDI, Volumatic®, respiratory system, LDA measurement technique.

WIT Transactions on Biomedicine and Health, Vol 17,
www.witpress.com, ISSN 1743-3525 (on-line)
doi:10.2495/BIO130031

1 Introduction

Asthma is a disease that affects a large percentage of the world population. There is no age group particularly affected but it is more worrying for children. For the treatment of this condition, inhalers are commonly used which allow the pulmonary deposition of drugs. There are many types of devices such as dry powder inhalers (DPIs), nebulizers or pMDIs. As a rule, pMDIs are commonly used because of their size, price and ease of use.

However, these devices are not fully effective, which leads to the usage of expansion chambers (commonly called spacers) attached to pMDIs to improve the efficiency of drug deposition. There are several spacers in the market and the Volumatic® is the most widely used because, besides being the one with the best results, it is also the one with a lower price for consumers. For this reason, Volumatic® has been studied to be able to improve its effectiveness.

Taking then into account the importance of this type of device, priority has been given to this type of study. There are several studies that computationally simulate the distribution of the fluid inside them with the objective of optimizing these devices. This study is important in order to understand which variations exist inside the spacer for the design of new devices (possibly with different geometries, sizes and mechanisms) in order to increase drug deposition in the lungs by inhalation.

However, it is important to know if these simulations are in agreement with what happens in reality, so it is important to compare the simulated values with those obtained experimentally.

Thus, a mechanism was designed and built that simulates the respiratory cycle, so it was possible to obtain conditions similar to those employed in the various simulation models that have been part of the team's work at the University of Minho in this area, combined with LDA techniques to analyse the flow inside the spacer device.

The above technique uses a high precision and high power laser, which inspires some caution to the user, both at a financial (due to the high cost of the sensor and its controller), and at a physiological level (if the user inadvertently looks into the laser, there is a high risk of blindness). This laser uses two beams of light, one blue and the other green, oriented perpendicularly to obtain spatial information for determining vector maps, which will be interpreted by dedicated software to obtain specific values of particles' speed.

The Volumatic® is a spacer that, due to its geometry, has recirculation zones (in the central zone of the spacer), as others with linear displacement. The analysis will be carried out on the central axis of the spacer, on the region near the walls, and in the middle region of these two, in order to analyse the trend of the particles' displacement inside the chamber.

2 Clinical perspective

Asthma is a chronic disease that affects a large percentage of the world population, making it a public health problem on which a lot of focus is given to soften its effects. All social classes, genders and ages suffer from this disease equally, although children and the elderly require more care [1].

The difficulty in the administration of drugs for treating asthma is related to the trouble of administering a minimum amount of drug that will achieve the therapeutic dose in the target organ; minimizing its side effects, and spacers are the devices commonly used in order to increase effectiveness [2].

The acquired data is only relative to the inhalation period, since a non-return valve (to prevent air to enter the spacer during the exhalation phase) is present in the nozzle area.

3 Initial parameters

As previously mentioned, the major objective of the designed system would be the duplication of the respiratory cycle, with an output flow close to real human flow, to observe not only the period where the highest speed occurs (named peak inhalation), but also to observe and analyse the exhalation period.

3.1 Experimental parameters

The first analysis was aimed at evaluating the performance of drug delivery by Ventilan® (inhaler) when coupled to three spacers, including the Volumatic®, using a simulated respiratory tract [3].

In addition to this analysis, simulations were also carried out using CFD tools (the Fluent™ software was used) to analyse the flow inside the Volumatic® spacer. For this numerical analysis it was necessary to establish a function corresponding to the periodic breathing cycle [3]

$$v\ (\mathrm{m/s}) = 6.458 \times \sin(1.571\ t) \tag{1}$$

The maximum value of 6.458 m/s is observed at 1 s at the nozzle, resulting in a null value for the instants between 2 and 4 seconds [4–5].

The developed assembly to simulate the breathing cycle used throughout this work was first designed by Rebelo [4]. This experimental system will be presented in the following section.

4 Experimental system

Although the experimental system itself, adopted in this study, was functional, it had to be adapted and optimized for the values of the speed, since they were not close to the parameters used in previous studies carried out and supervised by the authors.

Thus, it was necessary to modify some of its components, in order to obtain a flow rate as close as possible to the ones simulated computationally.

4.1 Components

The system will have several components, from the input position of particles in the system (or seeding), to the fan. Safety was also considered; protecting the user from inhaling harmful substances, as well as from looking directly at the laser (which, if misused, as mentioned, can cause blindness) – see Figure 1.

Figure 1: Schematic representation of the experimental system simulation of the respiratory cycle, adopted from [4].

It was also essential to have a force being exerted on the studied fluid, either as a result of the gravity or as a mechanism capable of acting upon it. In this case, a fan (capable of developing different speeds) was used to control the force being exerted as well as the intended respiratory flow.

So that the particles dispersed could not be released into the environment, and thus be harmful to the user, an extraction system was coupled to the experimental respiratory simulation system – see again Figure 1. The laboratory where the tests were carried out (at the Department of Mechanical Engineering, University of Minho) was equipped with an adequate fume exhaustion system, and it was used to blow the fluids and extract the particles being tested.

Table 1: Components of the experimental system.

Seeding	Nebulizer
Spacer	Volumatic®
Valve – Stepper motor	Inspiration/Expiration
Ventilator	Flow control with located throttle
Exhaustion	Particles of the sprayed material
Laser	LDA (Laser Doppler Anemometry)
Software	BSA Flow Manager®

The ventilator was connected to a tube about 70 cm long and with an internal diameter of 4.2 cm, being the spacer placed at one end, therefore it was necessary to obtain the values of 0.72 m/s, corresponding to the air flow observed in normal adult breathing.

In order to actually simulate the respiratory cycle, it was necessary to build a mechanism to control the ventilator, to generate the movement of inhalation and exhalation. To this end, a one-way valve was placed at about 20 cm from the fan, connected to a stepper motor programmed to operate according to the respiratory

www.witpress.com, ISSN 1743-3525 (on-line)

cycle: during inhalation, from 0 to 2 s, it would be opened (being fully opened during the first second), and during exhalation, from 2 to 4 s, it would be closed.

To reduce and regulate the speed on a smaller scale, it was also necessary to use a choke near the ventilator, in order to obtain the desired flow of 60 L/min used in the studies simulated computationally.

4.2 Limitations

Although the system has been designed and built to simulate the entire respiratory cycle, due to some limitations in manufacturing the parts needed, it was not possible to obtain a feasible system for the period of exhalation, i.e., where there is no flow within the system. To solve this situation, a valve that opens and closes, according to the programmed stepper motor, was added to the system; nevertheless it was not made and adapted for the inside of the tube, and a small gap between this parts could not be eliminated. Therefore, and although there is a decrease in the flow at the instant when the valve is closed, it does not completely block the flow as would be expected during the exhalation period.

4.3 LDA

The technique used to measure the velocity of the particles is based on the information collected by the reflection of light emitted by two different bundles, each one responsible for getting the dislocation in the same perpendicular axes, and these values are then interpreted by a set of filters and converters that are part of the overall measurement [5].

The analysis of the system will have only two dimensions; however, this technique can be extended to get a more detailed analysis in 3D, and thus build a virtual model of the flow inside the spacer. It can be designed so that images are created, or even analyse the texture of some surfaces, as long as there are enough lasers to carry out this task.

This technique has the disadvantage of relying on the introduction of particles in the flow. Since the analysis of the flow is based on the study of the particles' movement, it is of great importance to make sure that they also move with fluid, so that the final results describe the behaviour of the fluid properly and accurately.

On the other hand, this technique not only has disadvantages, but also has advantages; the most relevant for this case is the fact that it is a non-intrusive technique since there is no change in the flow and the measurement is based on linearization and stabilization of electromagnetic waves and as these do not change the physical factors (temperature or pressure, for example), the response of LDA to the speed of the particles is completely linear [6].

5 Test conditions

Although the term particles has been mentioned before, we need to take into account which ones are to be used because, as mentioned, the whole technique is based on the fact that there is reflection of light; if this phenomenon cannot be present, any velocity value can be obtained.

www.witpress.com, ISSN 1743-3525 (on-line)

5.1 Laser position

Initially, this study would be based on the analysis of fluid movement at the centre of the spacer, however, it was important to extend it to frontier areas and other intermediate zones in order to have a more complete analysis of the flow – see Figure 2. This technique is very accurate, and the intersection of the two lasers at the location needed to get values is of utmost importance.

To ease this process, the laser was coupled to a base whose the position could be adjusted in three directions (with a resolution of up to a tenth of a millimeter). Thus, it was possible to set the sensor in all positions needed to measure the particles, in the frontier positions, and also in the central part of the spacer.

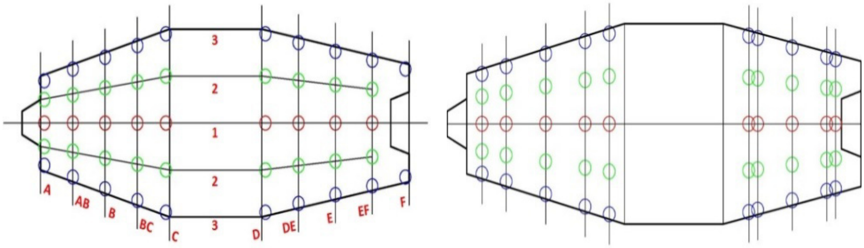

Figure 2: Map of the positions analysed inside the Volumatic® initially (left) and final (right).

5.2 Optical access

The position of the laser had to be changed, and a barrier was placed between the position of measurement and the laser. As the whole system depends on an optical phenomenon, and if any barrier with a certain angle is placed in the measurement range, there will be a refraction of light that will change the location of the intersection point.

5.3 Particles

To test the laser operation, water particles were nebulized. (No special care was considered for this experiment, since there was no danger to the user in the case of exhalation.) Thus, the parameters that could be changed and used to configure and reconfigure the system could be understood, and, therefore, to define their correlation with the obtained results.

After this analysis, the barrier system was introduced (while using the system to simulate the respiratory cycle), changing the water particles for oil particles, since the water particles were dispersed and evaporated within the system during the experiments.

In terms of efficiency of data collection, there was no variation related to the fluid change. Nevertheless, it was an important analysis, in order to obtain a greater number of particles circulating and also to increase the system validation.

6 Experimental tests

As mentioned before, there were several conditions tested in order to increase the level of knowledge about the system, and each variation introduced has increased the level of complexity of the test.

The parameters modified were all related to the configuration of the laser sensor to obtain feasible results, and the lens were initially defined as "fully opened", as well as the high values of sensitivity and signal gain.

6.1 Initial tests

The first tested condition was with vaporized water in the nebulizer, and with the laser sensor measuring the particles' velocity (Figure 3 – left). In this case, the largest possible parameter's range was tested, and, since there was no barrier, it would also be possible to eliminate a number of values. That is, if with no barrier it was not possible to obtain a rate of validation and/or acquisition of significant values, it would not be necessary to impose those same parameters in the following tests.

Figure 3: Assembly of the system in different stages: Initially with nebulizer (left), with the top of the Volumatic® (centre), and the final assembly (right).

Afterwards, a part of Volumatic® was placed on the nebulizer (Figure 3 – centre), in order to observe the changes that occurred in data acquisition with the introduction of a barrier.

The fluid was then changed, as mentioned previously, because the water evaporated and did not allow the acquisition of any kind of information about the particles' flow inside the tube or the final position of the spacer (Figure 3 – right).

6.2 Final assembly with defined parameters

At this stage, the ideal parameters were found and, therefore, no more variations were tested. The optimal parameters were obtained, as in the previous analysis, and those were used had a better correlation between the rate of validation and data acquisition.

www.witpress.com, ISSN 1743-3525 (on-line)

7 Analysis and discussion of results

7.1 Initial tests

7.1.1 Tests with water

It was basically not possible to collect any information for 500 V and 800 V supply voltage (sensitivity) of the laser; increasing the voltage to 1000 V, it was then possible to obtain results, i.e., the system was already beginning to measure the displacement of the particles even with a reduced lens aperture, without any barriers in the system. Using the system with barriers, it was only possible to obtain useful data for high values of signal gain, and with the lens “wide opened”.

For the following tests it was considered that the same signal gain ranges would be tested with a supply voltage higher than 1000 V.

7.1.2 Tests with oil

This change did not produce any significant variations regarding the behaviour of particles in the flow; however, many of the tests could not be carried out, due to fluid accumulation in the area of the non-return valve of the Volumatic®.

This accumulation influenced the results, since the area of air flow to the outside environment was covered with the accumulated fluid. Every time this blocking effect occurred, the entire system needed to be disassembled and the spacer needed to be cleaned. The observed variations in the velocity values were to be expected since, as the values were gathered, changes were introduced to the system to approach the required value.

The system, besides being associated with the ventilator which promoted the force required to achieve the desired fluid speed, was also connected to the exhaustion system of the laboratory, which also induced an additional force that had to be considered in the final value.

Thus, it was necessary to obtain a good relationship between the rate of validation and the data acquisition speed – 1600 V offered the best relationship in terms of sensitivity. For a voltage of 1400 V, the value of data acquisition was low (30 samples/s), although there was a validation rate of 96% to 10 dB. For 1800 V the highest value obtained was 123 samples/s, with only 85% of validation rate.

7.2 Volumatic® analysis

Based on the previous tests, it was possible to define the ideal conditions for the analysis of the Volumatic® spacer. To ease the analysis, the spacer was divided between the top, where the nozzle is located, and the lower zone. As in previous tests, which determined the optimal parameters for this analysis, oil particles were dispersed.

7.2.1 Analysis at the central axis

The results obtained at the centerline of the Volumatic® spacer (see Table 2) were, mostly, those which were expected to happen during the inhalation period.

As mentioned previously, the moment being considered is when the inhalation is at its maximum peak, that is, where the highest speed is observed. A comparison to be made with the previous work has to meet this important detail.

Table 2: Volumatic® values obtained in the central axis (velocities in m/s).

	Pos. A	Pos B	Pos. C	Pos. D	Pos. E	Pos. F
LDA1 (Y)	0.261	0.022	-0.049	0.084	-0.133	-0.048
LDA2 (X)	0.585	0.226	0.241	0.678	0.254	0.804
Vector	0.641	0.227	0.245	0.683	0.287	0.805

Analysing Table 2, it appears that the velocity is basically in one direction (X, which is the longitudinal direction of the spacer, where Y is the perpendicular direction), whereas the remaining values are all quite small. This scenario only changes in Position A, which is closest to the nozzle, where there were probably several flows and particles that crashed into the valve (and more likely to go up), which may support the scenario already discussed regarding the accumulation of fluids in the bottom of the valve.

As mentioned before, these values are as expected, since it was possible to verify that in the entry area of the fluid there was an increase of the particles' velocity, decreasing as approaching the valve (up to Point B). A value not expected was observed at Position E; although this occurrence is not clear to the authors, it still does not contradict the simulations carried out so far, or the polynomial trend depicted in Figure 4.

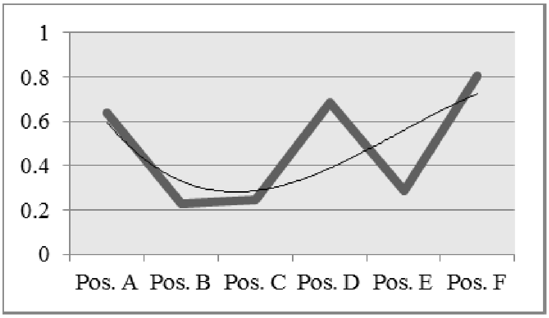

Figure 4: Illustration of speed on the central axis of the Volumatic® (velocities in m/s).

7.2.2 Analysis of the frontier areas and intermediate zones

These results will now be considered in relation to their behaviour (regarding the movement direction) and its amplitude, in relation to what is expected to occur from the simulations. Near the walls, as seen in Figure 5, there is a lower particles' velocity, as well as a huge recirculation zone at the central area of the spacer.

Although it was designed to observe a symmetrical behaviour with respect to the central axis of the spacer, to create two symmetrical parts, it can be observed that the obtained values vary a little. This behaviour was not expected, but, as previously suggested, this may be due to the fact that, inside the tube, the flow is not stable and there is some turbulence, creating an asymmetric “inhalation” or even small fluctuations in conjunction with the valve problem mentioned above. These may have some direct influence on the results. Nonetheless, based on the values for the two halves, and creating an average value of the results (after reversing the values of one side, so they do not cancel, because it was necessary to create a mirror effect), it was possible to build Tables 4 to 7 that show the final result.

Table 3: Summary of the results of the top part of the Volumatic® on the intermediate line (Line 2) (velocities in m/s).

	Pos. A	**Pos AB**	**Pos. B**	**Pos. BC**	**Pos. C**
LDA1 (Y)	0.014	0.012	0.047	-0.021	0.040
LDA2 (X)	0.560	0.035	0.103	0.092	0.031
Vector	0.560	0.037	0.113	0.095	0.051

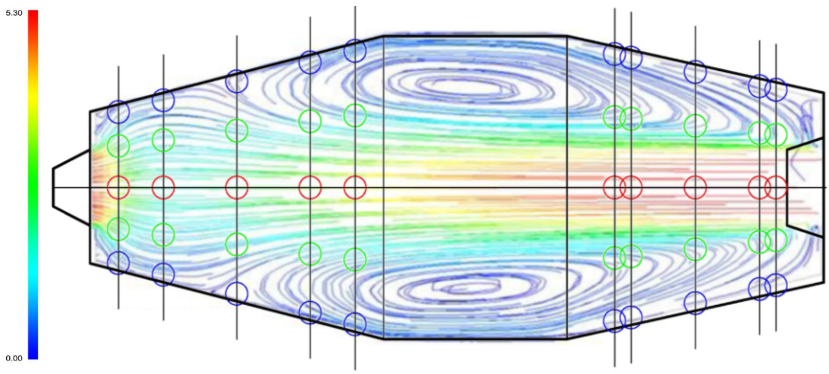

Figure 5: Overlap of the results obtained in [8] to map the location of the points examined.

With the data collected was possible to build a new scheme with the motion direction of the particles – see Figure 6. Something that was not expected to find was the high velocities near the walls in the X direction, since in the simulations they were characterized by low velocity values. In the simulations the velocities in the recirculation zones are low – see Figure 5, which shows the pathlines in each of the analysed points.

At the line level 2 (intermediate), although higher values were expected for the positions AB-BC-B-C, its direction stands in accordance with the simulations, except for BC on the Y axis (this variation is so small that it can be neglected). Position A, which is the closest to the nozzle, is the one where the

Table 4: Summary of the results of the top part of the Volumatic® on the frontier line (Line 3) (velocities in m/s).

	Pos. A	Pos AB	Pos. B	Pos. BC	Pos. C
LDA1 (Y)	-0.065	-0.025	0.044	-0.171	0.035
LDA2 (X)	0.034	0.119	-0.137	-0.396	-0.623
Vector	0.073	0.121	0.144	0.432	0.624

Table 5: Summary of the results of the bottom part of the Volumatic® on the intermediate line (Line 2) (velocities in m/s).

	Pos. D	Pos DE	Pos. E	Pos. EF	Pos. F
LDA1 (Y)	-0.107	-0.203	-0.056	0.153	-0.075
LDA2 (X)	-0.012	-0.012	-0.161	-0.032	0.121
Vector	0.107	0.203	0.171	0.157	0.142

Table 6: Summary of the results of the bottom part of the Volumatic® on the frontier line (Line 3) (velocities in m/s).

	Pos. D	Pos DE	Pos. E	Pos. EF	Pos. F
LDA1 (Y)	-0.147	-0.203	-0.196	-0.091	-0.022
LDA2 (X)	-0.525	-0.012	-0.139	-0.113	0.350
Vector	0.545	0.203	0.241	0.145	0.351

velocity in Y is close to 0 m/s, as seen in the simulations, as in the X direction which is high. For the following sets of Line 2, i.e., for the points D-E-DE-EF-F, only the EF comes with a direction (Y) out of what would be expected. Interestingly, at the central axis, the same abnormality occurred at the same point, it is possible to achieve consistency between the results.

Analyzing the area near the wall (Line 3), as already mentioned, the values were also higher than expected, but the direction was in accordance with the simulated results, except for Position BC. Passing from AB to point B, the difference between the particles that are moving forward to the nozzle and the ones that take the opposite direction, to create the recirculation already referred at the center of the spacer (near the walls), can be observed.

On the opposite side, near the entrance, the same recirculation phenomenon is also observed (in Position F – Line 3, it is possible to notice the reversal of the direction of the particles to the nozzle). Even so, the velocity is greater closer to the center of the spacer (Position A to C); this is due to the forces exerted, where all particles not moving in the nozzle then move to re-enter the stream of fluid.

Data collection in the center of the Volumatic® was not planned, since there were no variations in the geometry and the velocity profile was kept the same. However, it would not be possible to collect any results along the center line of the spacer.

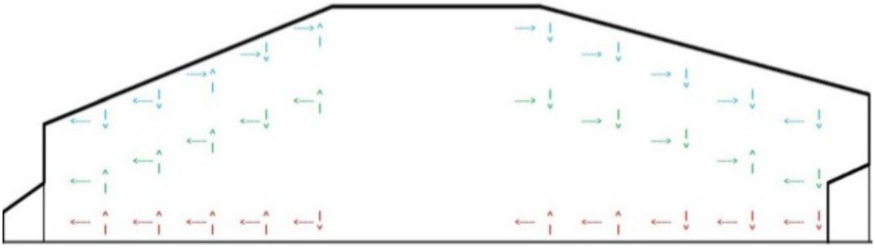

Figure 6: Scheme of the flow direction at each point analyzed in the Volumatic®.

This was related to the thickness of the wall of the spacer, not allowing the system to collect the light reflected from the particles, which lead to an adjustment of the positions to analyze – as shown in Figure 2.

Analysis of the particles' velocity was also planned, just after the valve (i.e., within the nozzle), but again no information could be obtained about that area. This was due to the geometry and thickness of the wall: the light beams could not cross this area, and there was not enough light reflected back.

8 Conclusions

The main objective of this work was to validate the studies undertaken so far, at the University of Minho, on the simulation of the flow inside the Volumatic® spacer. This study was also based on the use of a mechanical system, which was designed and developed specifically to duplicate the human respiratory cycle.

The experimentally obtained results were compared to those obtained in the simulations, and it is possible to conclude that the trend is the same as observed before and according to what was expected.

Apart from some differences that could be noticed, which can be addressed to the limitations highlighted in section 4, the experimental procedure herein proposed can be quite suitable to analyze the effectiveness of different spacers. During the course of this work it was possible to:

- Assemble and test the simulation mechanism of the respiratory cycle;
- Prove the existence of recirculation zones inside the Volumatic® spacer;
- Validate the numerical simulations carried out previously by the authors, where the trend of the fluids' movement inside the spacer was verified.

References

[1] Abreu, Sofia *et al.*; "Necessidade do estudo de câmaras de expansão para utilização em crianças asmáticas" 5º Congresso Luso-Moçambicano de Engenharia, Maputo, 2008.

[2] Miller, M. R.; Bright, P.; "Differences in output from corticosteroid inhalers used with a volumatic spacer" European Respiratory Journal, ERS Journals Ltd (1995), ISSN 0903-1936.

[3] Abreu, Sofia; "Estudo de diferentes câmaras de expansão para inaladores pressurizados "Dissertation of the Integrated Masters in Biomedical Engineering, Braga: Universidade do Minho, 2007.
[4] Rebelo, Rita; "Estudo e Análise CFD da Câmara de Expansão Volumatic®" Dissertation of the Integrated Masters in Biomedical Engineering, Braga: Universidade do Minho, 2009.
[5] Dynamics, Dantec Laser Doppler Anemometry – measurement principles, Dantec Dynamics – Laser Optical Measurement Systems and Sensors, Accessed on the 2nd November 2010, http://www.dantecdynamics.com /Default.aspx?ID=1046.
[6] Loureiro, J. B. R.; Pinho, F. T.; "Fundamentos de Anemometria Laser-Doppler" [Book Section] // Turbulência/Book Author Freire Atila P. Silva, Ilha Anderson e Colaço Marcelo J. – Rio de Janeiro: Associação Brasileira de Ciências e Engenharia Mecânica, ABCM, 2006.
[7] Falcão, Ricardo; "Optimização de Spacers" Dissertation of the Integrated Masters in Biomedical Engineering, Braga: Universidade do Minho, 2009.