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ORIGINAL PAPER

Performance evaluation of a new mobile air-treatment technology at-rest and under normal work conditions in a conventional hematology room

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Abstract

Invasive fungal infections incidence in patients with hematological malignancies is increasing. Air treatment remains an essential preventive measure. Guidelines state that high-risk patients should be housed in units equipped with High-Efficiency Particulate Air filtration. Mobile air-treatment devices may be considered as alternatives or as a complement to the ventilation system. We assessed the decontamination performances of a new mobile air-treatment device in a conventional hematology room. This device connected or not to a plenum combining Ultra-Low Particulate Air filtration and non-thermal catalysis process has been evaluated with or without healthcare activities (one sampling at-rest and triplicate samplings in activity). Environmental particulate, airborne and surface fungal and total mesophilic flora (TMF) samplings were performed with a total of 1800 min of particles counting, 144 air and 240 surface samplings. At-rest, both devices achieved a 2-log decrease of airborne particles, ISO 4 being the maximal particle class reached under the plenum. Whatever the healthcare activities and the location in the room, ISO 7 was the maximal particle class reached. TMF and fungal air contamination were lower during healthcare activities when the air portable cleaners were running. The bed was the area the least contaminated in the room. No differences were observed for surface contamination. This work provides arguments of the efficacy of a new mobile air-treatment device to decrease particle counts and airborne bioburden in real-life conditions. Studies have yet to be conducted to document the impact of these devices on the risk of invasive aspergillosis in immunocompromised patients.

Keywords Mobile air- treatment unit · Hematology · Invasive aspergillosis · Environmental samplings

1 Introduction

Control of the bioburden in the air is essential to lower the nosocomial infection risk in healthcare facilities, especially in operating theaters or in high-risk units housing immunocompromised patients**.** These infections are associated with significant morbidity, mortality and medical costs. Therefore, the prevention of patient's exposure to airborne pathogens remains a major challenge.

Operating rooms and cleanrooms for high-risk patients in hematology units fill the same need for strict environmental control. In France the ventilation must comply with the Standard NF S 90–351. In operating rooms, the matter concerning the use of laminar or turbulent airflow for prevention of surgical site infections remains unresolved [1]. Building and high risk area where cares are delivered to patients at high-risk should be equipped with High-Efficiency Particulate Air (HEPA) filtration combined with positive

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pressure (>15 Pascal) and an air exchange rate above 20 volumes per hour [2].

The number of immunocompromised patients is constantly increasing this last decade with an increasing incidence of invasive fungal infections (IFIs), especially invasive pulmonary aspergillosis (IA) in hematology patients [3]. *Aspergillus* species are filamentous fungi ubiquitously found in the environment [4]. Even if there is no agreement on a threshold of spore concentration beyond which a significant risk of IA occurs, the room environment around high-risk patients has to be maintained as free as possible from fungal spores [5–7].

High-risk patients may be transferred to other units, due to their health condition, where the ventilation system does not usually apply the standards of air treatment. Construction works have also been reported to be responsible for IA outbreaks [8]. Therefore, there is a need for devices to supply or improve the control of airborne contamination for high-risk patients. Portable air-treatment systems based on HEPA filtration and microbiological destruction have been used in hematology units over the past years to lower the airborne fungal burden including during construction or renovation works [7–10].

Based on these reports, The French Society for Hospital Hygiene advised the use of these portable devices, ideally made up of an overhead plenum with curtains suspended down from the plenum, as an alternative for decreasing the airborne contamination only when the air handling system is unavailable, or during high risk periods [2]. Although many portable systems have been developed, there is no substantial evidence that they reduce IA incidence. Additionally, the environmental impact of the devices to control the bioburden in the air was poorly studied during healthcare activities that generate a significant amount of airborne contamination. The measure of this bioburden can be evaluated by particle measure or culture of the total mesophilic and fungal flora [5]. Despite there is no significant correlation between particle measure and the amount of culturable total mesophilic flora (TMF), these parameters are usually used to measure the performances of the air handling system and to evaluate the quality of the surfaces cleaning.

The main objective of our study was to assess the particle and microbiological decontamination performances of a new technology using or not a plenum (laminar air flow vs turbulent flow), with or without healthcare activities in a conventional hematology room.

2 Materials and methods

2.1 Background and setting

Immunocompromised patients at high-risk of IA (allogeneic hematopoietic stem cell transplantation (HSCT) recipients and patients receiving induction chemotherapy for acute leukemia) are treated in the adult hematology department of the Cancer institute of Saint-Etienne (Institut de Cancérologie de la Loire Lucien Neuwirth, France). During renovation works, the adult hematology unit moved, at the end of March 2016, to another building to ensure that protective measures against fungal contamination were maintained. This new temporary 12-bed adult unit was located on the 5th floor of the main building of the University Hospital of Saint-Etienne. It was separated from other units by a locked access at the entrance (Fig. 1a). For the purposes of this study, only one room has been equipped with the two mobile air cleaners tested. The room volume was calculated at 66m^3 with sealed windows and a door that led directly to the corridor. The room received air treated coming from the central Heating, Ventilation, Air-conditioning and Cooling system including HEPA filters for each room but without positive pressure and with a very low air exchange rate of 2 volumes per hour. As a rule, in order to be allowed to house high-risk patients, including HSCT recipients, several other portable air-treatment cleaners (AirInSpace®, Montigny le Bretonneux, France) have been placed in corridors and other rooms, as depicted on Fig. 1a. Thus, without healthcare activities the baseline air handling level met the ISO Class 8 cleanrooms requirement in corridors [11].

2.2 Portable air-treatment units evaluated

2.2.1 R4000™ (AER technologies®, saint-Grégoire, France)

The R4000 unit is a mobile air-treatment device that can deliver treated air at 4000m^3 of air per hour. Briefly, the technology combines filtration with pre-filters, adsorbent filter and Ultra-Low Penetration Air (ULPA) filter U15, and micro-organisms destruction thanks to a non-thermal catalystic reactor associated with UV-C lamps. One of the mount of UV-C lamps has been disabled during the study period for reducing uncomfortable heat generation. In the tested room, this unit was placed in the corner facing the bathroom's door in order to optimize room and bathroom coverage (Fig. 1b).

2.2.2 Air supply ceiling

The technology used for the R4000™ can be connected to a plenum placed 2.03 m above the floor. Once decontaminated, air exiting the column after passing through the adsorbent filter is directed into a plenum where a HEPA filter is located. Unlike the R4000™ column alone, the air supply ceiling has no ULPA filter. Treated air is then delivered using laminar airflow over the bed. No curtains are suspended. One of the mount of UV-C has also been disabled for that device during the whole study period.

Fig. 1 Map of the adult hematology unit (**a**) and of the test room (**b**). Small red rectangles stand for Plasmair® units. Green rectangles stand for Immunair® units. The hatched area shown in Fig. b is for the air supply ceiling over the bed. The airborne particulate and microbiological sampling locations are denoted by the letter A, and the surface microbiological sampling locations are denoted by the letter S. HSCT, hematopoietic stem cell transplantation recipients

Both used devices operated at 600m^3 per hour and 1000m^3 per hour for the night and day settings, respectively. The room setting with the mobile devices is depicted in Fig. 1b.

2.3 Experimental design

During the first part of the study, performance evaluation of the mobile air-treatment devices was conducted without any patient or staff member in the room but healthcare activities were maintained for other patients in the unit. Tests were performed over 3 discontinuous days, each day with one condition: inactive mobile devices, running R4000™ but inactive air supply ceiling, inactive R4000™ but running air supply ceiling. Several weeks separated these conditions.

The second part of the study evaluated the performance of the mobile air-treatment devices with patients hospitalized in the room. Tests were carried out with 3 different patients at low risk for IA, hospitalized over 3 consecutive days for each patient [12] at the beginning and at the end of August, and in January. During the first day, both devices remained turned off until 6:00 pm, which corresponds to the time at which R4000™ was started up for next night and day running. On the second day, R4000™ was switched off at 4:00 pm and the air supply ceiling was turned on at 6:00 pm until the next day.

2.4 Sampling

On each test day, both particle and microbiological sampling were performed consecutively: particle sampling started 20 min after routine biocleaning during the morning. Microbiological air sampling was performed followed by surface sampling afterwards. Mobile units, particle and microorganism samples position in the room are displayed in Fig. 1b. The number of air sampling locations was determined by calculating the square root of the room surface area, which was 20.76m^2.

2.4.1 Particulate sampling

The concentrations of airborne particles with a diameter higher than 0.3 μm (P03), 0.5 μm (P05), 1 μm(P1) and 5 μm(P5) were counted using an Optical Particle Counter (Aerotrak® TSI, Shoreview, Minnesota, USA) in accordance with ISO 21501-4 standard [5]. The particle counter was placed 1.10 m above the floor except for the bed location where it was placed above the adjustable overbed table at 1.30 m from the floor, operating at a constant flow rate of 28.3 L of air per minute. The counter had a programmable delayed starter of 5 min to avoid any disturbing turbulence due to the presence of the operator.

At-rest, without patients, airborne particles counts were taken in 6 different locations in the room continuously over a 25-min period for each location in order to determine the mean concentration of particles at each location.

During healthcare activites, with patients and healthcare workers, airborne particle counter recorded at the same 6 places as before, 25 times consecutively over 1-min period at each place in the room to reflect the changes in particle levels due to normal work activities in the room. After hand hygiene, the operator wore disposable surgical mask, cap and gown and stood motionless in the room reporting all activities and movements, in order to correlate activities and their impact on particle level variations. One airborne particle measure was performed in the adjacent corridor nearby the Plasmair® unit (AirInSpace, Montigny-le-Bretonneux, France) over 1-min period repeated 25 times.

2.4.2 Airborne microorganisms sampling

Air samples were collected by impaction with a Sampl'air™ biocollector (AES Blue Line, Biomérieux, Marcy l'Etoile, France) loaded with Sabouraud-Chloramphenicol agar plates (Becton Dickinson, Heidelberg, Germany) and standard plates-count-agar (Oxoid, Dardilly, France) dishes for quantitative and qualitative identification of filamentous fungi, and (TMF) count determination respectively. For each sample, 0.5 m^3 of air was collected from a height of 1 m above the floor, at 100 L/min for 5 min. As a control, one air sample was taken in the adjacent corridor. Sampling locations were the same than those for particles measures. The amount of micro-organisms culture in the air was determined in terms of colony-forming-unit (CFU)/m^3.

2.4.3 Surface microorganisms sampling

Fungal contamination on surfaces was evaluated by wiping a sterile dry cotton-tipped swab covering approximately 25 cm^2 over the following material surfaces: the bedside table, the phone, the adjustable overbed table, the chair, the sink, the baseboard, the window sill, the top of the R4000™ unit, the conductor rail system, and a shelf in the closet.

Surface samples were also collected for TMF evaluation with 55 mm diameter Count-Tact® Agar (Biomerieux, Marcy l'Etoile, France) dishes applied for 20 sec on each surface. Cotton-tipped swabs were rubbed on Sabouraud-Chloramphenicol agar plates. Sabouraud plates were incubated for 24 h at 35 °C and then maintained at 25 °C for 6 days, with daily screening for fungal growth. Molds were identified to the genus/species level based upon macroscopic and microscopic morphological characteristics when the development of colonies was sufficient.

Petri standard plate-count agar and Count-Tact® Agar dishes, used to monitor the TMF, were maintained at 22 °C for 5 days, with daily screening. The colonies that grew out were counted but not identified.

2.5 Ethics

This study was approved by the hospital ethics committee (IRB 332016/CHUSTE) of the University hospital of Saint-Etienne, France. As the functional tests were performed for research purpose to evaluate the performance of the two mobile units before possibly using them with high-risk patients for preventing invasive fungal infections, only low-risk patients were included in the study.

2.6 Outcomes

Particle concentrations were expressed as the number of particles per cubic meter. The concentrations of 0.3 μm, 0.5 μm, 1 μm and 5 μm particles were categorized according to the upper limits allowed in cleanrooms classified as Class 5, 6, 7, 8 or 9 according to the ISO 14644-1 standard, even for the measures with healthcare activities [11].

Since the new hematology unit had a low exchange air rate with no positive pressure, a threshold of 10 CFU/m^3 was set to define positivity of TMF in air samples. It was based on the bacteriological purity M10 classification required for a level 3 risk area according to the standard NF S90–351 [5].

A Cut off value of 5 CFU/25 cm^2 for TMF contamination on surface was specified, based on the French Regional guidelines for environment control in care facilities [13].

The target value for fungal contamination in air and on surfaces was below 1 CFU/m^3 and 1 CFU/25 cm^2, respectively.

2.7 Statistical analysis

Statistical analysis was performed with the SPPS software (version 20.0, Chicago, IL, USA).

Quantitative variables were presented as the number of particles counts classified according to the ISO 14644-1 limits standards and the concentration of TMF and fungal flora on surfaces and the air classified as defined above. When appropriate, the mean (±standard deviation) and median (interquartile range) values were calculated. Qualitative variables were presented as the number of measures and percentages. For each analyze, measures performed with one of the mobile devices were compared to measures performed without them. Student tests were used for comparison of mean particulate concentration. Chi squared and fisher's exact tests were used to compare categorical variables. The Kruskall-Wallis test was performed to compare the mean concentrations of airborne and surface microbiological contamination according to the type of mobile air-treatment device. The p values below 0.05 were considered statistically significant.

3 Results

The study was conducted between August 2016 and January 2017.

3.1 Particle monitoring

At-rest, inside the room, in the absence of any portable air cleaner, global airborne particle count did not exceed the ISO 14644 Standard limits for ISO 8 cleanrooms, ISO 7 at the bed location and ISO 8 at the bathroom location. When R4000™ unit was operational, airborne particle level did not rise above the ISO 6 class inside the room, including the bathroom. Lastly, when the air supply ceiling was running, the particle level was limited to the ISO 6 class inside the room

including the bathroom whereas the airborne particle level did not rise above Class 4 at the bed location. ISO 7 was the maximal particle class reached in the corridor, irrespective of the use of the mobile devices. The particle count in the corridor constituted a positive control.

During healthcare activities, as depicted in Table 1, without any portable devices, the concentration of particles reached the ISO 7 and ISO 8 classes, wherever it was recorded in the room. We observed a major airborne particulate contamination in January without portable devices, with P03 reaching 2.5×10^7 particles/m^3. When the portable air cleaners were running, almost no particle samples exceeded the maximum level for Class 7. The particulate contamination recorded above the bed reached mostly the ISO 6 class, and even ranged between Class 4 and Class 5 when the air supply ceiling was on. Figure 2a and b illustrate some activities that generated particulate contamination. For example, when a nurse handled the infusion stand in the middle of the room, we noticed a particle peak over the bed barely exceeding the limit for ISO 7 when the R4000 unit was running. As soon as the nurse left the room, and the patient remained calm, we observed a rapid decrease of particulate concentration. It took less than 10 min to remove 90% of particles (Fig. 2a).

3.2 Microbiological contamination

Table 2 displays proportion of positive samples as defined in the Methods section and the concentration of both TMF and fungal contamination over surfaces and in the air.

We noticed that almost all the air samples performed without any portable air cleaner displayed concentrations of TMF above 10 CFU/ m^3. The proportion of positive samples, during healthcare activities, was significantly lower when R4000^{TM} unit or the air supply ceiling were used ($p < 0.001$ and $p < 0.001$ respectively) with a significant reduction by half of the air sample density. When the portable devices were running, the concentrations of TMF flora were lower compared to the samples collected without these devices reaching a quantity below 10 CFU/ m^3 in 2/3 of experiments without patient and during healthcare activities. With the R4000 unit, only 1 out of 8 air samples collected over the bed was contaminated with 42 CFU/m^3 while the portable air cleaners were operational. The area of the bed was the place the least frequently contaminated in the air. The bathroom location even without any healthcare activity had the same proportion of positive air samples for TMF contamination in the 3 conditions. When the air supply ceiling was running, the bed location was the only place in the room that met the criteria of permitted TMF concentration. The surrounding room and the bathroom never met these criteria.

Surfaces displayed a comparable proportion of TMF contamination regardless of the use of a portable air cleaner at-rest. During healthcare activities, surfaces were significantly less frequently contaminated when the air supply ceiling was used, ranging from 30 to 57%. Room surfaces with indirect contact with the patient (conductor rail system, baseboard, window sill) were slightly contaminated.

Only one air sample was positive for fungal contamination at-rest and it appears to be a non-pathogenic mold from *Penicillium* species, found in the bathroom when mobile devices were switched off. No fungi were detected in the air when mobile devices were running at-rest.

One CFU/25 cm^2 of *Mucor* sp. was found once on the conductor rail system when no mobile devices were running. One surface with no direct contact with patient was positive for *Penicillium* sp. on the day of R4000™ unit's use and on the day of air supply ceiling's use. One CFU/25cm^2 of *Alternaria* sp. was recovered at-rest on the shelf while the air supply ceiling was running.

At the same period of January while we noticed a major particulate contamination in the room, we detected 6 positive air samples for *Aspergillus fumigatus* when no portable devices were used during healthcare activities. All the sampling places of the room were contaminated. Three of these samples were also positive for *Penicillium* sp. and one was also positive for *Aspergillus versicolor* and *Penicillium* sp. The next morning, when R4000 was running, no samples were positive for *Aspergillus fumigatus* but one CFU/m^3 of *Aspergillus caesiellu* was detected in the middle of the room. No fungi were discovered in the air when the air supply ceiling was used. No *Aspergillus* contamination was recovered from surfaces.

When portable devices were used, surfaces with direct contact with the patient were never contaminated with a pathogenic mold. The phone sample was positive once for *Rhodotorula glutinis* without any portable devices during healthcare activities.

3.3 Comfort assessment

The two mobile devices were relatively well accepted by both patients and nursing staff. However, the most frequent complaint was the discomfort as a result of the heat generated by the units, especially at high outdoor temperatures. The room temperature rose of 3 to 5 degrees Celsius, even reaching 35 °C when the air temperature in the corridor was around 27 °C. Noise and room's obstruction were not reported as annoying.

4 Discussion

This preliminary but innovative study provides some arguments for the effectiveness of a new mobile device in terms of environmental control. Our work evaluated particle, TMF

Table 1 Distribution of particulate samplings according to concentration of particles during healthcare activities

	Without any mobile device (n=450)			R4000^{TM} unit (n=450)			Air supply ceiling (n=450)			Corridor (n=225)	Air supply ceiling washout (n=150)
P03 (particles/m^3)	Global	Bed (n=75)	Bathroom (n=150)	Global	Bed (n=75)	Bathroom (n=150)	Global	Bed (n=75)	Bathroom (n=150)		
Median	3.7 x10^5			1.7 x10^4			1.8 x10^4			3.1 x 10^4	2.2 x10^4
Mean (±SD)	8.2 x 10^6 (±1,1x10^7)			2 x 10^5 (±2,3x10^5)			2.6 x10^5 (±4,1x10^5)			2.05 x 10^5 (±3,7x10^5)	2.7 x10^4 5 (±2,1x10^4)
- <1.02 x10^3 (ISO4)	0	0	0	0	0	0	39 (8.7%)	39 (52%)	0	0	24 (16%)
- 1.02 x 10^3 to 1.02 x 10^4 (ISO5)	0	0	0	177 (39.3%)	10 (13.3%)	49 (32.7%)	127 (28.2%)	31 (41.3%)	50 (33.3%)	4 (1.8%)	1 (0.7%)
- 1.02 x 10^4 to 1.02 x 10^5 (ISO6)	0	0	0	120 (26.7%)	40 (53.3%)	51 (34%)	157 (34.9%)	4 (5.3%)	50 (33.3%)	110 (48.9%)	103 (68.7%)
- 1.02 x 10^5 to 1.02 x 10^6 (ISO7)	295 (65.6%)	45 (60%)	100 (66.7%)	153 (34%)	25 (33.3%)	50 (33.3%)	74 (16.4%)	1 (1.3%)	20 (13.3%)	102 (45.3%)	22 (14.7%)
- >1.02 x 10^6 (ISO8)	155 (34.4%)	30 (40%)	50 (33.3%)	0	0	0	53 (11.8%)	0	30 (20%)	9 (4%)	0
P05 (particles/m^3)											
Median	1.8 x 10^5			9.3 x 10^3			9.7 x10^3			1.6 x 10^4	1.1 x10^4
Mean (±SD)	9.4 x 10^5 (±1,1x10^6)			3.5 x 10^4 (±4,2x10^4)			3.2 x10^4 (±4,2x10^4)			7,2 x 10^4 (±6,7x10^4)	1.5 x10^4 (±1,3x10^4)
- <3.5 x 10^2 (ISO4)	0	0	0	0	0	0	28 (6.2%)	28 (37.3%)	0	0	24 (16%)
- 3.5 x 10^2 to 3.5 x 10^3 (ISO5)	0	0	0	114 (25.3%)	5 (6.7%)	23 (15.3%)	92 (20.4%)	45 (60%)	26 (17.3%)	0	3 (2%)
- 3.5 x 10^3 to 3.5 x 10^4 (ISO6)	0	0	0	179 (39.8%)	44 (58.7%)	77 (51.3%)	200 (44.4%)	1 (1.3%)	74 (49.3%)	113 (50.2%)	101 (67.3%)
- 3.5 x 10^4 to 3.5 x 10^5 (ISO7)	288 (64%)	38 (50.7%)	100 (66.7%)	157 (34.9%)	26 (34.7%)	50 (33.3%)	130 (29%)	1 (1.3%)	50 (33.3%)	111 (49.3%)	22 (14.7%)
- >3.5 x 10^5 (ISO8)	162 (36%)	37 (49.3%)	50 (33.3%)	0	0	0	0	0	0	1 (0.5%)	0
P1 (particles/m^3)											
Median	8.2 x10^4			4.8 x10^3			4.6 x10^3			7.5 10^3	5.1 x10^3
Mean (±SD)	2 x10^5 (±1,9x10^5)			9.5 x10^3 (±9,9x10^3)			8.6 x10^3 (±8,8x10^3)			2,1 x10^4 (±1,6x10^4)	7,2 x10^3 (±6,5x10^3)
- <8.3 x 10^1 (ISO4)	0	0	0	0	0	0	16 (3.6%)	16 (21.3%)	0	0	24 (16%)
- 8.3 x 10^1 to 8.3 x 10^2 (ISO5)	0	0	0	24 (5.3%)	0	3 (2%)	82 (18.2%)	56 (74.7%)	3 (2%)	0	1 (0.7%)
- 8.3 x 10^2 to 8.3 x 10^3 (ISO6)	0	0	0	240 (53.3%)	47 (62.7%)	80 (53.3%)	176 (39.1%)	2 (2.7%)	77 (51.3%)	85 (37.8%)	72 (48%)

Table 1 (continued)

	Without any mobile device (n=450)			R4000^{TM} unit (n=450)			Air supply ceiling (n=450)			Corridor (n=225)	Air supply ceiling washout (n=150)
- 8.3 x 10^3 to 8.3 x 10^4 (ISO7)	229 (50.8%)	3 (4%)	81 (54%)	186 (41.3%)	28 (37.3%)	67 (44.7%)	176 (39.1%)	1 (1.3%)	70 (46.7%)	140 (62.2%)	53 (35.3%)
- >8.3 x 10^4 (ISO8)	221 (49.2%)	72 (96%)	69 (46%)	0	0	0	0	0	0	0	0
P5 (particles/m^3)											
Median	2.5 x10^3			1.4 x10^2			1.4 x 10^2			3.2 x10^2	4.2 x10^2
Mean (±SD)	3.6 x10^3 (±3,2x$10^{3)}$			3.5 x10^2 (±9x10^2)			2.3 x10^2 (±2,7x10^2)			5.9 x 10^2 (±5,3x10^2)	7 x10^2 (±7x10^2)
- <2.9 x 10^1 (ISO5)	0	0	0	20 (4.4%)	1 (1.3%)	4 (2.7%)	83 (18.4%)	63 (84%)	7 (4.7%)	1 (0.5%)	24 (16%)
- 2.9 x 10^1 to 2.9 x 10^2 (ISO6)	0	0	0	324 (72%)	58 (77.3%)	106 (70.7%)	232 (51.6%)	12 (16%)	81 (54%)	72 (32%)	31 (20.7%)
- 2.9 x 10^2 to 2.9 x 10^3 (ISO7)	259 (57.5%)	44 (58.7%)	82 (54.7%)	99 (22%)	16 (21.3%)	40 (26.7%)	135 (30%)	0	62 (41.3%)	151 (67%)	94 (62.6%)
- >2.9 x 10^3 (ISO8)	191 (42.5%)	31 (41.3%)	68 (45.3%)	7 (1.6%)	0	0	0	0	0	1 (0.5%)	1 (0.7%)

P03, 0.3µm particles concentration; P05, 0.5µm particles concentration; P1, 1µm particles concentration ; P5, 5µm particles concentration ; SD, Standard deviation

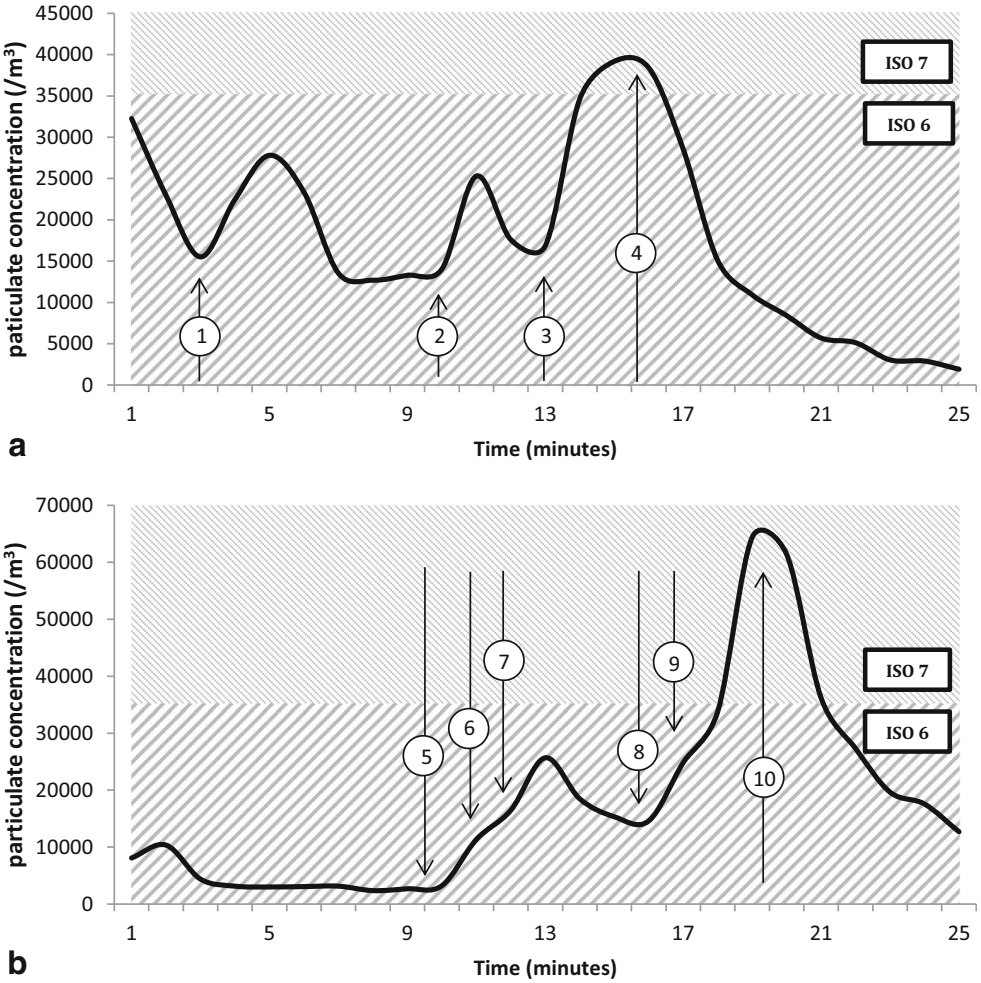

Fig. 2 Impact of some healthcare activities on particles concentration of 0.5 μm size. **a**: particulate sampling performed at bed location with running R4000™. **b**: particulate sampling performed in the middle of the room with running air supply ceiling. 1: two nurses come in the room to replace a bandage; 2: the door is open and closed twice in a minute; 3: nurses take care of the infusion stand; 4: nurses leave the room; 5: a caregiver comes in the room; 6: the caregiver leaves the room; 7: the caregiver comes back to take patient's blood pressure; 8: the caregiver moves in the bathroom; 9: the caregiver leaves the bathroom; 10: the caregiver leaves the room

and fungal flora contamination, at-rest and under normal working conditions, reflecting real-life in a patient room.

Despite the less-than-optimal conditions in our temporary adult hematology unit, namely a very low air change rate, the absence of positive-pressure ventilation and with no air lock anteroom, we were able to point out both particulate and microbiological results. We could achieve with the R4000™ unit and also with the air supply ceiling a 2-log decrease in the resting state of airborne particles in the test room, including the bathroom. A 3-log decrease was even made possible at the bed location under the running plenum at-rest. When patients were hospitalized in the test room, whatever the healthcare activities and the place in the room, ISO 7 was the maximal particle class reached, when particle counts were interpreted according to the ISO 16144-1 airborne particulate cleanliness classes. We were even able to measure, in absence of any consecutive activity, the time necessary to reach a 90% decontaminate of 0.5 μm particles, rising up to 10 min at bed location under the running plenum. Finally, the bed seemed to be the only place in the room with the air supply ceiling where the airborne TMF burden is the most contained at-rest, but also when a patient is hospitalized with healthcare activities.

Control of particle contamination by air-handling system during healthcare activities has mainly been studied in operating rooms with staff equipped with operating block uniforms including masks, or in cleanrooms of pharmaceutical industries [14]. Evaluated activities were limited to walking, remaining seated or stretching exercises. The rare studies concerning particle generation in a hematology unit were limited to the impact of biocleaning [15, 16]. In our study, patients hospitalized were at low-risk for IA, so nursing and medical staff did not wear any mask or gown. Thus, what makes our study truly unique is that the particle results are representative of real life in a conventional hospital room. As we showed on Fig. 2, peaks of particles are generated during nursing care, but mobile air-treatment systems can decrease the magnitude of these peaks, despite the activities of nursing staff. We are aware that these measures are not standardized and require measures of particle decontamination kinetics at-rest, to respond to the NF S90–351 standard [5].

Table 2 Environmental microbiological and fungal air and surface contamination with and without patients, under three air-treatment conditions

		Samples without patient								
		Without mobile air treatment			R4000™			Air supply ceiling		
		Air (n=6) (CFU/m^3)	Surface (n=10) (CFU/25cm^2)	Corridor Air (n=1) (CFU/m^3)	Air (n=6) (CFU/m^3)	Surface (n=10) (CFU/25cm^2)	Corridor Air (n=1) (CFU/m^3)	Air (n=6) (CFU/m^3)	Surface (n=10) (CFU/25cm^2)	Corridor Air (n=1) (CFU/m^3)
TMF contamination	Positive samples	100%	20%	100%	17%¶	20%	100%	50%	10%	100%
	Median (min-max)	25 (10-30)	1 (0-98)		4 (0-58)	0 (0-56)		9 (0-28)	0.5 (0-7)	
	Mean concentration ± SD	23±6.9	11.9 ±30.4	42	12.3 ±22.6	6.5 ±17.5	76	11.3 ±11.9	1.3 ±2.2	18
Fungal contamination	Positive samples	17%	20%	0%	0%	20%	0%	0%	10%	0%
	Median (min-max)	0 (0-1)	0 (0-1)	0	0	0 (0-2)	0	0	0 (0-1)	0
	Mean concentration ±SD	0.17 ±0.4	0.20 ±0.4	0	0	0.20 ±0.6	0	0	0.10 ±0.3	0
		Samples with patient								
		Without mobile air treatment			R4000™			Air supply ceiling		
		Air (n=18) (CFU/m^3)	Surface (n=30) (CFU/25cm^2)	Corridor Air (n=3) (CFU/m^3)	Air (n=18) (CFU/m^3)	Surface (n=30) (CFU/25cm^2)	Corridor Air (n=3) (CFU/m^3)	Air (n=18) (CFU/m^3)	Surface (n=30) (CFU/25cm^2)	Corridor Air (n=3) (CFU/m^3)
TMF contamination	Positive samples	94%	57%	100%	33%¶	47%	100%	39%¶	30%¶	100%
	Median (min-max)	22 (6-60)	6 (0-300)	40 (14-68)	6 (0-100)	3 (0-180)	34 (34-56)	9 (0-42)	4 (0-86)	36 (16-114)
	Mean concentration ± SD	35.9 ±21.4	18.3 ±54.5	40.6 ±22	17.4 ±26	13.5 ±32.4	41.3 ±10.3	14 ±13.5	12 ±19.5	55.3 ±42.2
Fungal contamination	Positive samples	44%	7%	33%	17%¶	3%	0%	0%¶	7%	66%
	Median (min-max)	0 (0-50)	0 (0-3)	0 (0-1)	0 (0-1)	0 (0-1)	0	0	0 (0-1)	1 (0-2)
	Mean concentration ±SD	14.7 ±22.7	0.13 ±0.5	0.3 ±0.5	0.16 ±0.4	0.03 ±0.2	0	0	0.06 ±0.3	1 ±0.8

CFU, colony-forming unit; SD, standard deviation; TMF, total mesophilic flora

¶ Statistical significant results

The TMF is not usually pathogenic but measures of TMF constitute an usual indicator to evaluate the quality of the air that depends on the efficacy of air handling system and surface cleansing [5]. Repeated quantifications of this indicator allowed to describe a lower rate of air contamination in the test room, whatever the activities, when the portable air cleaner devices were running in accordance with the results of particle counts. The measures of fungal flora were also quantified but pathogenic fungi were identified. Actually, even with very low fungal environmental bioburden outbreaks have been reported [7]. Therefore, the aim to achieve is the absence of pathogenic fungus in the room of immunocompromised patients. As for the TMF contamination we observed less air samples contaminated with fungal flora when the air portable devices were used. Conversely, no difference was noticed regarding the surfaces contamination with or without use of these devices.

We faced a very high airborne particle baseline levels in January, on the same day as *Aspergillus fumigatus* was recovered in air samples of the whole room. It is well-established that there is an association between higher particle counts and fungal detection even if there is no determined threshold [17]. No *Aspergillus fumigatus* colony was found the next morning when the R4000™ unit was running or the day after with the air supply ceiling. These data suggest that this burst of fungal contamination could have been controlled with the mobile air-handling systems, even if we cannot exclude a natural elimination of this contamination by the air handling system. Portable air mobile treatement systems reduce the risk of fungal exposure for immunocompromised patients. This efficacy was demonstrated especially during renovation works generating *Aspergillus* contamination [8]. We did not find any explanation for this burst of contamination: no close renovation works in and in the surroundings of the unit were reported. No IA was documented in the unit during this time period. Additionally, we cannot exclude a transient contamination because we performed only 6 air samples of 0.5 m3 during the same experiment.

Airborne TMF measures at-rest and during normal work conditions displayed lower airborne contamination in the room when using the R4000™. This contamination was even lower under the running plenum with a laminar airflow. The bed area was the most protected area in the room. The highest TMF contamination was observed in the bathroom. It has been shown that bathrooms in protected units could be a source of fungal contamination whereas rooms were in accordance with recommendations [18]. The lack of protection in bathrooms could be attributed to the distance between mobile units and the bathroom. Indeed, even if the bathroom's door remained open to optimize the bathroom's coverage, it was 3 to 4.5 m away from the mobile devices. Although the flow of air as it emerges from the R4000™ unit or from the plenum may be laminar, it becomes turbulent over and around objects and personnel in the room. Moreover, bathrooms may have defective siphons that require frequent filling. Water flush constitutes also a source of aerosolized droplets.

There are several limitations in this study. First of all, caution should be taken with interpretation of our results because of the limited number of samples, especially for experimental conditions at-rest. We didn't perform as much samples as we had planned. Indeed, as the hematology unit was operational, the room could not be cleared often enough because of the high demand for a timely turnover by medical management staff. Thus, experiments at-rest could not be repeated three times. Because of the real-life design of the study we were not able to control all conditions influencing airborne contamination as for experimental study. Secondly, a very short "wash-out" period of 2 h was considered between the two mobile devices use during the second part of the study. We can argue that the air supply ceiling may have benefited of the efficacy of the R4000™ unit used the day before. Indeed, the use of the air supply ceiling was associated with a reduction of the surface TMF contamination, whereas the rest of the surface fungal and TMF analyses with R4000™ were not different from baseline levels. We can assume that the airborne results with the air supply ceiling have been influenced by this short wash-out period, and that the airborne contamination didn't return to baseline levels before the use of the air supply ceiling. To evaluate that effect, we performed another measure under normal working conditions, beginning with the use of air supply ceiling. Particulate samplings didn't reveal a greater particles concentration, except for 5 μm particles (Table 1). All the airborne and surface fungal samples remained sterile. However, the airborne TMF concentration appeared to be significantly higher than when the air supply ceiling was running on the day after the R4000™ unit activity ($p = 0.02$). Hence, we can hypothesize that microbiological results when the air supply ceiling was running may have been biased by the absence of consequent "wash-out" period. Thirdly, in France there is no agreement regarding the optimal incubation conditions for fungal recovery [19]. We cannot exclude that the incubation period at 35 °C used in our study could have been too short for optimal growth of *Aspergillus spp*. We used the standard method promoted by our laboratory to survey units at high risk of IA in the University hospital and in our cancer institute. Lastly, experimental conditions provided for the study were not ideal. In order to minimize heat generation and preserve patient's well-being, one of the mount of UV-C lamps has been disabled. No standardized particle decontamination kinetic has been done. It would have required producing an artificial contamination of the room air, supposedly to be occupied few days later.

The first data concerning use of mobile air-treatment systems can be situated around 1980 in onco-hematology units.

Until 2007, mobile devices tested could only perform air filtration through HEPA filters. Subsequently, a novel technology originally developed for the International Space Station decontamination was used in hematological units [6–8]. These new units could not only filter air but also destroy microorganisms, thus preventing particle accumulation and microorganisms growth on HEPA filters. Most of the previous studies evaluating portable air-treatment systems mainly focused on fungal risk, and not so much on bacteriological or viral risk. An overview of studies looking for the impact of portable air-treatment systems on environmental contamination and on clinical risk of developing a fungal infection is provided in Supplementary Data. None of these studies was randomized. The results are difficult to compare because of the different surveillance methods and outcomes used. Eight of the 16 studies have been conducted in the context of aspergillosis outbreaks or renovation works [10, 20–26]. In these specific circumstances, all authors who performed environmental surveillance showed a significant reduction of airborne fungal contamination, including *Aspergillus* species, after installation of portable air-treatment devices in onco-hematology units. But it is not clear in these studies whether these results can be solely attributed to that implementation, since other measures were simultaneously taken, like application on surfaces of an antifungal biocide like copper-8-quinolinolate, patients' chemoprophylaxis or technical corrective actions. In only one study, the results were inconclusive and the authors did not recommend the use of their portable HEPA filtration device [27]. Some studies have included data from comparison of portable air-treatment units-equipped rooms and built-in ventilation rooms [9, 28]. Their findings support an increased efficiency of built-in ventilation in terms of airborne fungal exposure. Clinical impact of mobile air-treatment devices has been retrospectively evaluated in seven studies. Four of them concluded that use of mobile air-treatment devices was associated with a reduction of IA incidence and one of these studies showed a reduction of invasive fungal infections incidence. But these studies didn't have a high level of evidence and no data is available concerning mortality. Only one study compared efficiency of several mobile devices assessing the fungal decontamination of a room where 10^6 *Aspergillus niger* has been aerosolized [29]: Plasmair® unit was more rapidly effective than the other devices to reduce the airborne fungal concentration. It was suggested that it was because of its better airflow. In another study this device allowed to decrease the airborne fungal contamination in a pediatric onco-hematological ward [30]. The two units that we have tested have functioned at 1000m^3/h during the day, which is not the maximal attainable airflow. The limit that we found was the heat generation, especially when outdoor temperatures were already high in summer. With such airflow, noise was not considered by patients as a problem. On the basis of the information available at that time, mobile systems have only proved their ability to lower airborne fungal burden.

5 Conclusion

This experimental and preliminary study, mixing physical and microbiological measures at-rest and in activity, provides some arguments of the efficacy of a new mobile air-treatment technology to decrease particle counts and airborne bioburden in patient's environment. As described in this study and as recently stated by the French Society for Hospital Hygiene, it is possible to use portable air-treatment units when built-in ventilation is defective, or when renovation works are undertaken, in order to decrease *Aspergillus* exposure. Studies have yet to be conducted to document the impact of these devices on the risk of IA in immunocompromised patients.

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Compliance with ethical standards

Competing interests The authors declare no conflict of interest. The different stages of the study, including experimental design, sampling and analyses, were carried out in full independence of the mobile devices supplier company.

Research involving human participants and/or animals This study was approved by the hospital ethics committee (IRB 332016/CHUSTE) of the University hospital of Saint-Etienne, France.

Ethics approval and consent to participate Verbal consent of patients was obtained and the study was approved by the ethical committee.

Conflict of interest The authors declare that they have no competing of interests.

Abbreviations *HEPA*, High-Efficiency Particulate Air; *HSCT*, Hematopoietic Stem Cell Transplantation; *IA*, Invasive Aspergillosis; *IFI*, Invasive Fungal Infection; *TMF*, Total Mesophilic Flora; *ULPA*, Ultra-Low Penetration Air

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