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Safe-by-design strategies applied to scaffold hybrid manufacturing

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Abstract. The EU-project FAST (GA 685825) has developed a 3D printer machine prototype for the manufacture of bone implants (scaffolds), by merging masterbatches of biodegradable polymer poly(ethylene oxide)terephthalate/poly(butylene terephthalate) [PEOT/PBT] doped with nanofillers [reduced graphene oxide (rGO), hydroxyapatite (HA) and magnesium aluminium hydroxide ciprofloxacin hydrotalcite (LDH-CFX)], and atmospheric plasma technology. This paper focus on the safe design strategies identified by FAST to address the risk to health resulting from the potential airborne emission of nano-objects and their aggregates and agglomerates (NOAAs) by the 3D printer prototype, which might result in occupational exposures by inhalation. The work also includes measurements of airborne emissions and occupational exposures carried out during the verification stage of the prototype design. Nanofillers particles (rGO, n-HA, LDH-CFX) were not observed, neither at source nor in the working area, suggesting no release of free nanofillers to the air one they have been embedded in the polymer masterbatch. Additionally, the exposure in the workplace was far below the selected Occupational Exposure Levels (OELs), for total particle number concentration (PNC), dust, elemental carbon (EC) and volatile organic compounds (VOCs). The results showed that, when working with the current prototype in normal operation (for its intended use) and with controls enabled [enclosure with the doors closed and Local Exhaust Ventilation (LEV) activated], the emission from the machine and the worker's exposure to NOAAs are well controlled.

1. Motivation

The EU-project FAST [1] developed a 3D printer machine prototype for the manufacture of bone implants (scaffolds), highly customized to the patient at affordable cost. These artificial bones are made of a polymer composite enforced by a specific treatment of the implant's surface. Target fields of application of FAST scaffolds include treatment after bone trauma, tumour, infection, and non-union after fracture.

The most relevant nano-specific risk associated with the new FAST 3D printing prototype is the potential emission into the air of aerosols containing NOAAs, during the manufacture of scaffolds, as well as during other machine life cycle operations, such as maintenance, cleaning and adjustment. This can result in occupational inhalation exposures of NOAAs by workers. The source of potential airborne NOAAs are the nanofillers processed by the machine for the manufacture of scaffolds: reduced graphene oxide (rGO), hydroxyapatite (nHA) and magnesium aluminium hydroxide ciprofloxacin hydrotalcite-(LDH-CFX). In addition to NOAAs, other nanoparticulate contaminants and volatile organic compounds (VOCs) can be also emitted during the manufacturing process.

This paper focus on the safe design strategies identified by FAST to address the risk to health resulting from the potential airborne emission of NOAAs by the 3D printer prototype, which may result in occupational exposures by inhalation. The work also includes measurements of airborne emissions and occupational exposures, carried out by the project for the verification of the prototype design.

2. Introduction

Additive Manufacturing (AM) - also known as 3D Printing - is a manufacturing process that uses AM machinery - also known as 3D Printers - to make parts from 3D model data, usually layer upon layer [2,3]. The FAST 3D printer prototype is based on 3D fiber deposition, which is an extrusion-based AM technology [2]. Here, a polymer filament is heated and extruded through a nozzle to create an object. During the extrusion, the polymer filament is heated and degraded, producing a release of ultrafine particles (size less than 100 nm) and organic chemicals into the air. At FAST, 3D printing is combined with plasma in a single machine prototype. The plasma process is a well-known method for the synthesis of nanoparticulate powders. The ionized gases in the plasma produce decomposition reactions which lead to the formation of nanoparticles.

In recent years, AM processes and their possible health effects are attracting attention due to the increased use of this type of manufacturing machinery. With regard to extrusion-based 3D printers, the state of the art shows that heated filaments emitted large numbers of very small particles and volatile organic chemicals which could be breathed in [4,5,6,7,8,9,10,11,12,13,14,15,16,17,18,19,20,21,22]. Characteristics of these airborne emissions are variable, depending on the type of filament, materials involved, printer process, temperature and nozzle design amongst others [9,10,16,23]. The most common hazard associated was inhalation exposure, followed by dermal exposure [16,24]. The studies also showed that control measures as enclosures with air extraction reduce effectively the emissions [16,18,25,26,27]. To the best of our knowledge, we have not found a systematic research studying the emissions and exposures of 3D printers, combining printing and plasma stages, and using PEOT/PBT doped with nanofillers.

Manufacturers of 3D printers must ensure the compliance with the Machinery Directive (MD) [28], before placing them on the EU market. In particular, the essential health and safety requirement (EHSR) 1.5.13, refers to "the "*emissions of hazardous materials and substances produced by machinery*", where potential NOAAs air emissions as well other conventional pollutant emissions (e.g. VOCs, dust) are included. The FAST prototype is excluded from the application of the MD, until its placed on the market and/or put into service.

Besides the MD, other EU regulations may apply to the FAST-3D prototype, such as EU legislation on Medical Devices and chemicals, amongst others. In particular, AM machinery can be used to manufacture medical devices, which are within the scope of the Directive on Medical Devices [29]. This is the case of FAST, and consequently the scaffolds manufactured by the 3D printer must also meet the requirements of this legislation before being placed on the market. Finally, in the field of professional use of 3D printing machinery by workers at work, the OHS Directives apply.

Currently, European AM machinery manufacturers are supporting the design of 3D printers on general safety of machinery harmonized standards, because there is not yet a specific "type-c" standard on AM machinery [30]. In this sense, some non-harmonized standards published or under development by ISO/TC 261, CEN/TC 448 and ASTM/F42 technical standardization committees on AM, are also highly relevant, in particular those referring to health and safety issues of this technology [31,32,33].

3. Methodological approach

3.1 The FAST 3D prototype

The FAST 3D prototype manufacture scaffolds, by merging masterbatches of biodegradable polymer poly(ethylene oxide)terephthalate/poly(butylene terephthalate) [PEOT/PBT] doped with nanofillers [reduced graphene oxide (rGO), hydroxyapatite (HA) and magnesium aluminium hydroxide ciprofloxacin hydrotalcite (LDH-CFX)], and atmospheric plasma technology.

The prototype is based on 3D fiber deposition using material extrusion (ME). In this AM process, the biopolymer filament (PEOT/PBT) doped with nanofillers, is heated and extruded through a pressurized nozzle into the form of filaments, which solidify onto the build platform to construct the scaffold, layer upon layer. A relevant novelty of the FAST prototype is the combination of the scaffold printing and its subsequent functionalization by plasma, in a single machine. Plasma coating produces extremely thin layers that give coated scaffolds special properties.

The prototype includes two main modules: 1) the print pen module, a single-screw extruder system with two inlet reservoirs that contains the polymer nanocomposites (pellets); and 2) the plasma jet module, allowing the surface chemical functionalization of scaffolds. The prototype is enclosed in a methacrylate box, with local extraction ventilation (LEV) to avoid the release of fumes and particles to the lab (Figure 1).

The operating procedure consists of two main stages: 1) Printing stage: the process starts by heating the printer prototype previously filled with the masterbatches, for some minutes. When the printing temperature set point is arrived, the scaffold printing is performed for around 10 minutes. The LEV is off during this stage and the frontal door is sometimes opened for readjustments; 2) Plasma stage: once the scaffold is finished, the flow of plasma gases starts (N_2/Ar, 3-Aminopropyl trimethoxysilane precursor, APTMS) and the plasma is ignited. The plasma jet is located on the top of the printed for one minute; later the plasma jet is running over the scaffold surface for 5 minutes for functionalization. In this stage, the LEV is on and the door is kept closed during all the process. At the end of the day, the different printer parts are cleaned.

The FAST prototype is currently installed in a research laboratory at Maastricht University, with controlled mechanical ventilation and a room temperature of 22 ºC.

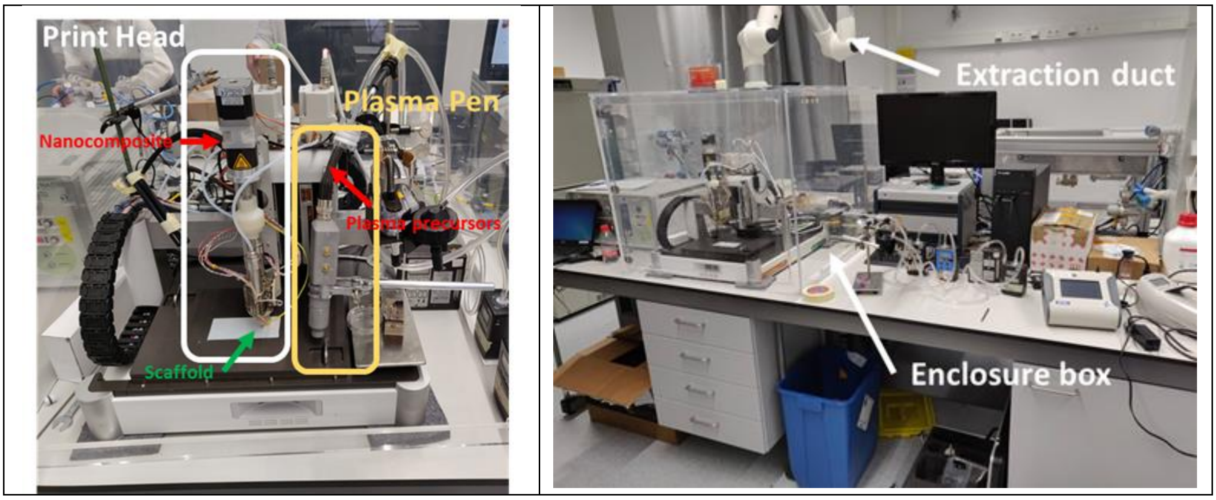

Figure 1. The FAST-3D prototype showing the two manufacturing modules, the print head and the plasma jet (left); and the enclosure box and the Local Exhaust Ventilation system – LEV (right).

3.2 Toxicity of nanofillers and masterbatches

The toxicology of nanofillers and masterbatches doped with them were studied by the project. rGO was the most toxic of the four nanofillers evaluated (see Table 1). The results also showed that the risks derived from the use of masterbatches were lower. Table 2 shows that the viability of MR5, Hep G2, THP1 and 3T3 cells exposed to net extracts of most of the masterbatches was higher than 70%. According to EN ISO 10993-5 [34], a reduction of cell viability for the highest concentration of the sample extract (100% extract) by more than 30%, is considered a cytotoxic effect. Although rGO was the most toxic of the four nanofillers analysed, the results suggest that once incorporated in the masterbatch, the risk derived from its use in the manufacturing process was greatly reduced (Table 2).

Further information on the toxicity of nanofillers and masterbatches evaluated by FAST can be found in references [35] and [36]. In addition, considerations about cell toxicity upon polymer degradation can be also found in reference [37].

Table 1. Toxicity assessment of nanofillers: summary of results obtained in some cytotoxicity assays (WST-1: WST-1 assay; NRU: Neutral Red Uptake assay; IC50: half maximal inhibitory concentration)

	Toxicity evaluation assay							
	WST1 (IC50 µg/ml)				NRU (IC50 µg/ml)			
Nanofillers	MR5	HepG2	THP1	3T3	MR5	HepG2	THP1	3T3
HA	303	482	>500	>500	>500	>500	>500	>500
ZrP	>500	>500	>500	>500	>500	>500	>500	>500
LDH	>500	338	100	>500	>500	>500	>500	>500
rGO	**22**	>500	**5**	>500	368	246	**63**	>500

Table 2. Toxicity assessment of masterbatches: summary of results obtained in some cytotoxicity assays (WST-1: WST-1 assay; NRU: Neutral Red Uptake assay)

	Toxicity evaluation assay							
	WST1 (% viability after exposing to net extract)				NRU (% viability after exposing to net extract)			
Masterbatch	MR5	HepG2	THP1	3T3	MR5	HepG2	THP1	3T3
LDH-CFX 5%	>70	>70	>70	>70	>70	>70	>70	>70
LDH-CFX 10%	>70	>70	>70	>70	>70	>70	>70	>70
LDH-CFX 20%	>70	>70	>70	>70	>70	>70	>70	>70
ZrP-GTM 5%	>70	>70	>70	>70	>70	>70	>70	>70
ZrP-GTM 10%	>70	>70	>70	>70	>70	>70	>70	>70
ZrP-GTM 20%	>70	>70	>70	>70	>70	>70	>70	>70
rGO 3%	>70	>70	**<70**	>70	>70	>70	>70	>70
rGO 10%	>70	>70	>70	>70	>70	>70	>70	>70
rGO 15%	>70	>70	>70	>70	>70	>70	>70	>70

3.3 Safe design approach for the FAST 3D printing prototype

The objective of a safe design of the FAST-3D printer with respect to the risks derived from the emission and exposure to NOAAs, should be to ensure the manufacture of scaffolds, keeping these risks adequately reduced. This objective can be achieved by the elimination of hazards, or by reducing the associated risk.

The map of strategies designed to achieve this objective has been inspired by the safety of machinery harmonized standards EN ISO 12100 and EN ISO 14123-1 [38,39]. This map (Table 3) considers a global safe design approach, where the set of protective measures is the combination of the measures implemented by the designer (part A of the table) and the user (part B).

3.4 Verification of the prototype

The verification of the prototype design was done by measuring airborne emissions and occupational exposures in two locations (source and working area), using a combination of portable DRIs for online PNC measurement in the range 10 nm to 10 µm (TSI CPC 3007 and TSI OPS 3330), and filter-based sampling for off-line analysis (total dust, EC, TEM VOCs) (Figure 2).

In general, the measurement strategy was based on the OECD tiered approach [36], by including the collection of information on the toxicology of the nanofillers (rGO, n-HA and LDH-CFX) and process characteristics (Tier 1), as well as the development of a basic measurement campaign using handled devices and filter sampling (Tier 2).

Figure 2. Different pictures of the FAST 3D prototype installed in the research laboratory of Maastricht University, showing the deployment of instrumentation for the measurement of emissions and exposures to NOAAs, during the verification stage of the prototype design.

Three tasks were monitored: Task 1 - Scaffold printing, Task 2 - Plasma functionalization and Task 3 - Printer cleaning. Emissions of the machine (inside and outside the enclosure) and occupational exposures (by inhalation) were measured using masterbatches of PEOT/PBT polymer, without nanofiller (control) and filled with rGO, HA and LDH-CFX. Measurements with each masterbatch were repeated twice to monitor and collect samples at the two locations: at source, inside the enclosure, to get information about the emissions from the process; and, in the operator working area, to characterise worker exposure in normal operation. In total, seven complete machine cycles were measured, two (source and work area) for each of the four masterbatches, except for the LDH-CFX, where measurements could only be made at source due to schedule limitations. At source measurements, the inlets to the DRIs and filter samplers were co-located inside the prototype enclosure and the LEV was turned off during all tasks. For working area measurements, the LEV was on during the plasma stage.

In addition to DRI measurements, sets of four simultaneous samples were collected during each of the measured machine cycles. The samples captured for the analysis of the total aerosol mass were collected on 37 mm PVC filters, those destined for the EC analysis on 25 mm pre-treated quartz filters, the samples for TEM on 25 mm polycarbonate filters and, finally, those for the analysis of VOCs in activated carbon tubes (TCA 100/50 mg). The standards used for the offline analysis were NIOSH 0500, NIOSH 5040, and OSHAS 7 [41,42,43].

The inference about potential occupational exposures was made by comparing the measurements in the working area, with substance specific and categorical OELs. The worst case was postulated, assuming that the entire sampled mass corresponded to the pollutant evaluated. OELs selected for the nanoparticulate range were: 40.000 particles/cm^3 for the total particle number concentration (PNC); 0,165 mg/m^3 for rGO (0,066 * WEL, TWA for graphite (respirable) is 2,5 mg/m^3); and 0,3 mg/m^3 for HA and LDH-CFX respectively (MAK values, respirable) [44,45,46].

In this work, sampling devices were not worn by the worker so as not to disturb its working procedures and comfort. Alternatively, they were located at a static point, in front of the printer enclosure, where the operator is usually located during the process. The operator wore conventional lab clothes, and gloves were used during the printing and cleaning tasks.

4. Results and discussion

4.1 Map of strategies for a safe design and operation of the FAST prototype, regarding the risk resulting from the emission of NOAAs

Table 3 shows the map of strategies for a safe design and operation of the FAST 3D printer prototype, regarding the risk to health resulting from the emission of NOAAs by the machine. This emission can result in occupational inhalation exposures of NOAAs by workers.

Regarding the strategies applied by the DESIGNER, inherently safe design strategies are always the first priority. They are aimed at eliminating hazards or reducing the associated risks, by changing the design or operating characteristics of the machine [38]. Examples of this type of measures proposed for the FAST prototype are: 1) the use of alternative nanofillers in the manufacturing process (this measure is conditioned by compliance with regulations on medical devices and chemicals); 2) the modification and improvement of the operating parameters of the process, to reduce emissions; 3) the design of operation, maintenance and cleaning sequences to minimize environmental, health and safety impacts.

Safeguards and complementary protective strategies are implemented when it has not been feasible to eliminate the hazard or reduce its associated risk sufficiently, using inherently safe design measures. Examples of this type of measures proposed for the FAST prototype are: 1) the enclosing of 3D printer and the installation of a LEV with filtration; 2) the interlocking of the enclosure doors with automatic monitoring and its connection with the safety-related parts of the control system, to prevent airborne hazardous emissions until doors are closed (e.g. with the plasma operating); and 3) the installation of the machine in a dedicated room.

After the implementation of inherently safe design and complementary protective strategies, the remaining residual risks are identified in the information for use of the machine. Examples of this type of measures proposed for the FAST prototype are: 1) the implementation of visual danger signals on the FAST prototype (e.g. hazardous emissions, use of PPEs, doors always closed), and 2) the elaboration of the Instruction Manual (IM) of the machine, describing among other: the intended use of the FAST-machine; the hazardous substances that can be generated by the process; the complementary protective measures to be taken at workplace by the end user (LEV connection; operating, maintenance and cleaning procedures, adequate PPEs and hygiene arrangements).

Strategies applied by the designer can be supplemented by USER strategies in the workplace, to cover the residual risks and achieve the maximum overall risk reduction. This user-strategy should rely strongly on information provided by the manufacturer, basically through the Instruction Manual. Some typical user-strategies in the workplace under the STOP principle proposed by FAST, not the only ones, focus on the implementation of additional engineering measures, organizational measures, PPEs and training.

Some strategies have already been implemented by the FAST prototype; others are still pending and may guide future improvements in the prototype, for the future placing on the market and professional use by workers.

Table 3. Map of strategies for a safe design and operation of the FAST prototype, regarding the risk resulting from the emission of NOAAs

A. DESIGNER STRATEGIES			
TYPE OF STRATEGY			MEASURES PROPOSED FOR THE FAST 3D PRINTING PROTOTYPE
Step 1 (First priority)	1. Inherently safe design strategies (“Pure” SbD strategies)		Alternative ENMs; conditioned by compliance with REACH, RoHS, RMD (EN ISO 10993) [47]. Modification / Improvement of the operating parameters of the machine (to reduce emissions); improved design of operation, maintenance and cleaning procedures to minimize EHS impacts.
Step 2 (Second priority)	2. Safeguarding and complementary protective strategies	2.1 Reduction of emission	Interlocking enclosure doors with automatic monitoring (EN ISO 14119) [48] and safety-related parts of control system (EN ISO 13849-1) [49], to prevent airborne hazardous emissions until doors are closed (e.g. with the plasma operating). Start command to LEV.
		2.2 Reduction by ventilation or other engineering means	Enclosing 3D printer + LEV + filtration, safety-related parts of control system (EN ISO 14123-1, EN ISO 13849-1) [39,49].
		2.3 Reduction of exposure by machinery operation or segregation	Dedicated room (EN ISO 14123-1) [39].
Step 3 (Third priority)	2. Information for use strategies		Warning of residual risks: visual danger signals (hazardous emissions, use of PPEs, doors always closed) (EN 61310) [50].
			Instruction Manual (IM) (EN ISO 20607:2019) [51]: intended use; hazardous substances that can be generated by the machine; complementary protective measures to be taken at workplaces [risk control system (machine-LEV); operating, maintenance and cleaning procedures; PPEs and hygiene arrangements].
B. USER STRATEGIES			
TYPE OF STRATEGY			MEASURES PROPOSED FOR THE FAST 3D PRINTING PROTOTYPE
STOP principle		**S**ubstitute/Modify	In agreement with recommendations provided by the manufacturer in the Instruction Manual (IM). Conformity with the intended use of the machine.
		Further **T**echnical measures	In agreement with recommendations provided by the manufacturer in the IM. Connection of the machine to a LEV system, if required. Portable vacuum unit for cleaning tasks.
		Organizational measures	In agreement with recommendations provided by the manufacturer in the IM. Safe working procedures for normal operation (Close enclosure doors) and cleaning/maintenance operations. Safety and health signs at work (Directive 92/58/EC) [52].
		Use of **P**PEs	In agreement with recommendations provided by the manufacturer in the IM. PPEs are required during operation, cleaning and maintenance operations (safety glasses, safety gloves, and respirator). Ensure proper maintenance of PPEs.

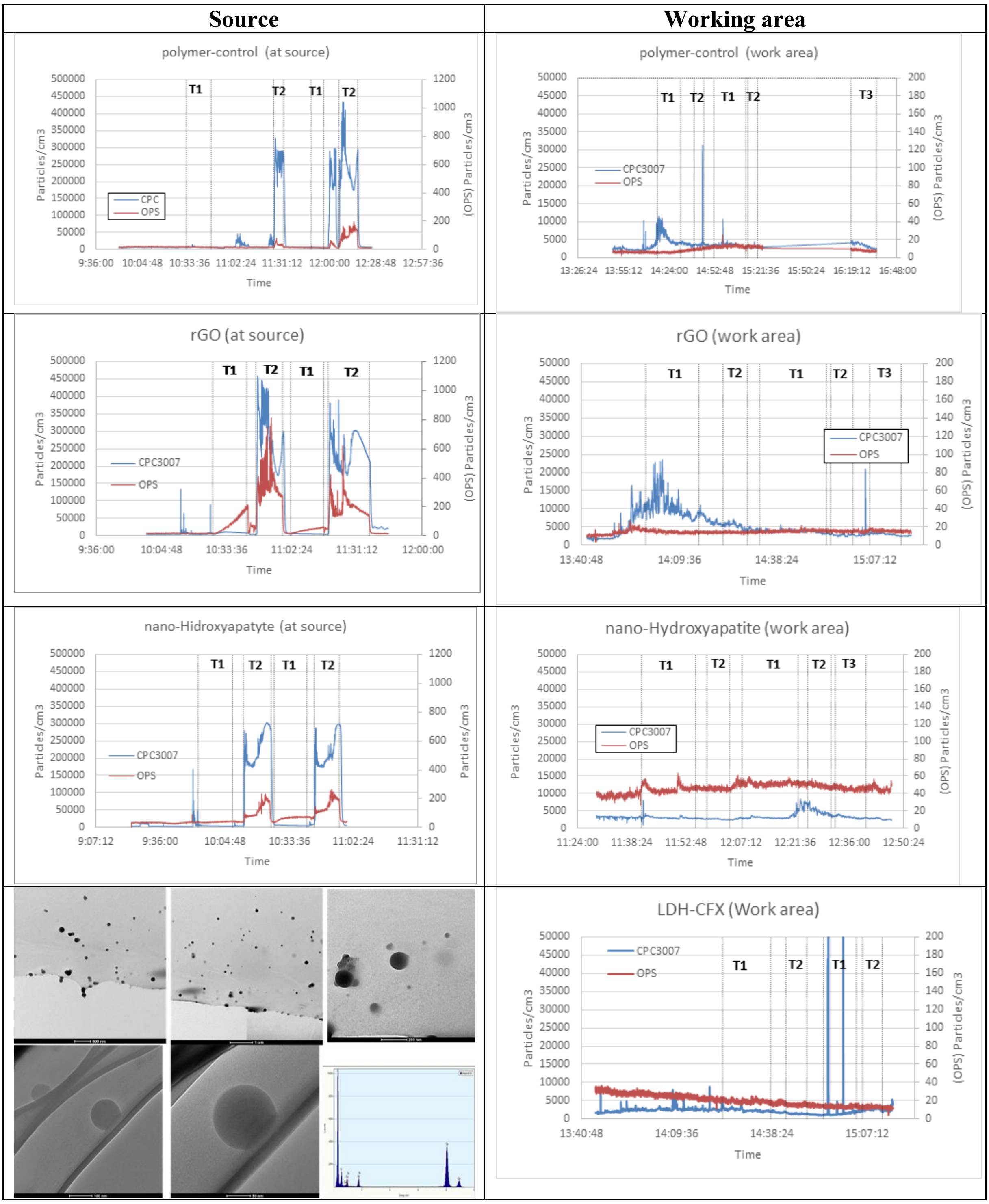

Figure 3. Time series (PNC, particles/cm^3) registered by DRIs, at source (left) and in the operator working area (right), during testing with masterbatches of PEOT/PBT, without nanofiller (control) and filled with rGO, HA and LDH-CFX (up to down). T1, T2 and T3 respectively identify the tasks of Printing, Plasma and Cleaning. TEM image shows spherical silica particles (20 nm and 200 nm) collected at source during the rGO test, which are suggested to be generated from the interaction of plasma with the gas precursor (APTMS).

4.2 Verification of the prototype design by measuring airborne emissions and occupational exposures.

- Air emissions of the machine prototype

Data at source, inside the enclosure of the 3D prototype, showed no releases of particles or a slight increase of PNC during the printing step, for all nanofillers tested (Figure 3). As reported in the literature [5,21], these ultrafine particles are probably condensates of organic compounds generated during the polymer heating and degradation.

Measurements taken at source showed that the plasma process produced a high number of nanoparticles, as expected. A high increase of PNC during the plasma process, above 250.000 particles/cm^3, has been measured (peak value exceeding 450.000 particles/cm^3). TEM analysis of the particles collected in the plasma stage, identified spherical particles smaller than 200 nm in all cases. The morphology and the composition (EDX) of these particles suggest that they are silica nanoparticles, produced during the plasma interaction with the amino-silane precursor gas (APTMS). Silica nanoparticles are currently synthesised in plasma reactors using organosilicon compounds.

No nanofillers particles (rGO, n-HA, LDH-CFX) were observed in any of the samples collected, suggesting no release of free nanofillers to the air once they have been embedded in the masterbatch.

- Occupational exposures by inhalation

Data collected in the working area, in normal operation, showed no increase in PNC from the background levels (Figure 3). The exposure is well below the categorical OEL of 40.000 particles/cm^3 selected, in all cases.

A summary of the average particle number concentration, at source and working area, for the different tested masterbatches (control, rGO, HA and LDFH-CFX) and stages of the manufacturing process (Printing, Plasma and Cleaning), can be shown in tables 4 and 5 at the end of the paper.

The analysis of filter samples showed that, in all cases, the total aerosol mass and the total EC mass were below the limit of detection (LOD).

Very few particles were observed in the samples collected at the working area. Their morphology and composition suggest that they are common particles found in the work environment. Nanofillers particles were not observed in any of the samples collected at the working area. Silica particles were also not observed, suggesting that these nanoparticles are not released to the working area when working in normal operation (enclosure of the prototype with the doors closed).

Finally, data on the levels of the four volatile organic compounds identified and measured (acetonitrile, toluene, acetone and ethanol) were well below applicable OELs. In any case, the source of these VOCs, quite common in the lab, is unclear and cannot be directly associated to 3D printing activities.

5. Conclusions and beyond

This paper summarizes the map of SbD strategies designed by the EU-project FAST, to address the risk to health resulting from the potential air emission of NOAAs by the FAST 3D printer prototype, during the manufacture of scaffolds and secondary operations; which may result in occupational exposures by inhalation. Some SbD strategies have already been implemented by the prototype. Others are still pending and may guide improvements to the machine for the future placing on the market and professional use by workers.

Measurements at source showed that the plasma stage produced a high number of nanoparticles, as expected. These particles are spherical particles, with a size between 20 and 200 nm. It is suggested that they are n-SiO_2 nanoparticles produced during the plasma interaction with the APTMS precursor gas.

Nanofiller particles (rGO, n-HA, LDH-CFX) were not observed, neither at source nor in the working area, suggesting no release of free nanofillers to the air one they have been embedded in the polymer masterbatch.

Silica nanoparticles generated during the plasma stage were not observed in the working area, suggesting no release of these nanoparticles when working in normal operation (enclosure of the prototype with the doors closed).

Additionally, the exposure in the workplace was far below the selected OELs for PNC, dust, EC and VOCs.

Measurements of emissions and exposures carried out during the project for the verification of the FAST 3D prototype design, demonstrated that - when working with the prototype for its intended use, following established manufacturing procedures, with the enclosure doors closed and the LEV activated - the emission of the machine and the worker's exposure to nanoparticles are well controlled.

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Table 4. Average concentrations of total particles (PNC, particles/cm^3) at SOURCE, for the different tested masterbatches (control, rGO, HA and LDFH-CFX) and stages of the manufacturing process (Printing, Plasma and Cleaning). The last two rows of the table, in capital letters, represent the average values calculated for the two main stages (Printing and Plasma), from the measured values of the individual tasks.

TSI CPC 3007	(10 nm – 1 µm)						SOURCE									
Masterbatch	**Control**				**rGO**				**n-HA**				**LDFH-CFX**			
Task	*Mean*	*SD*	*Max.*	*Min.*	*Mean*	*SD*	*Max.*	*Min.*	*Mean*	*SD*	*Max.*	*Min.*	*Mean*	*SD*	*Max.*	*Min.*
No activity	5911	548	7235	4560	4634	177	5472	4045	6474	3699	14034	3216	-	-	-	-
Printing 1	6644	1066	14898	5581	9355	1701	11958	4631	4724	899	12758	3679	-	-	-	
Printing 2	5293	519	9135	4415	5916	542	8343	4890	6240	787	9309	4904	-	-	-	-
Plasma 1	244155	73454	328854	12646	251496	119667	459221	4519	200109	58801	302427	4232	-	-	-	
Plasma 2	206672	62926	435648	9034	205821	90713	387223	4522	194938	63708	298669	8311	-	-	-	-
PRINTING	5969	838	14898	4415	7636	1262	11958	4631	5482	845	12758	3679	-	-	-	-
PLASMA	225414	71389	435648	9034	228659	106182	459221	4519	197524	61304	302427	4232	-	-	-	-
TSI OPS 3330	(300 nm – 10 µm)						**SOURCE**									
Masterbatch	**Control**				**rGO**				**HA**				**LDFH-CFX**			
Task	*Mean*	*SD*	*Max.*	*Min.*	*Mean*	*SD*	*Max.*	*Min.*	*Mean*	*SD*	*Max.*	*Min.*	*Mean*	*SD*	*Max.*	*Min.*
No activity	18	2	24	13	18	1	22	14	34	2	39	27	-	-	-	-
Printing 1	17	1	21	14	84	54	205	14	38	3	46	31	-	-	-	-
Printing 2	14	1	17	11	40	12	63	15	65	10	78	34	-	-	-	-
Plasma 1	35	12	80	13	325	112	809	98	101	25	234	39	-	-	-	
Plasma 2	86	14	198	12	198	80	620	45	138	20	266	66	-	-	-	-
PRINTING	16	1	21	11	62	39	205	14	52	7	78	31	-	-	-	-
PLASMA	61	14	198	12	262	97	809	45	120	23	266	39	-	-	-	-

Table 5. Average concentrations of total particles (PNC, particles/cm3) in the WORKING AREA, for the different tested masterbatches (control, rGO, HA and LDFH-CFX) and stages of the manufacturing process (Printing, Plasma and Cleaning). The last two rows of the table, in capital letters, represent the average values calculated for the two main stages (Printing and Plasma), from the measured values of the individual tasks.

TSI CPC 3007	(10 nm – 1 µm)						**WORKING AREA**									
Masterbatch	**Control**				**rGO**				**HA**				**LDFH-CFX**			
Task	*Mean*	*SD*	*Max.*	*Min.*	*Mean*	*SD*	*Max.*	*Min.*	*Mean*	*SD*	*Max.*	*Min.*	*Mean*	*SD*	*Max.*	*Min.*
No activity	2535	265	3447	962	1836	176	2258	1102	3224	238	3771	1565	2477	553	8860	1439
Printing 1	5768	1976	11575	3362	10415	3090	23597	6435	3110	347	8071	1009	2443	379	3818	1740
Printing 2	3571	562	10696	2687	3873	375	5634	2929	3234	584	7407	2644	2494	8452	135240	979
Plasma 1	4308	3561	31346	2882	5476	635	7293	3732	2711	100	2924	2415	1511	102	1882	1211
Plasma 2	2965	2965	255	4497	2919	229	3614	2254	5573	797	7906	3412	2647	269	3760	2007
Cleaning	3403	656	4868	2143	3095	349	4302	2357	3242	369	4310	2617	-	-	-	-
PRINTING	4670	1453	11575	2687	7144	2201	23597	2929	3172	480	8071	1009	2469	5982	135240	979
PLASMA	3637	2524	31346	2433	4198	477	7293	2254	4142	568	7906	2415	2079	203	3760	1211

TSI OPS 3330	(300 nm – 10 µm)						**WORKING AREA**									
Masterbatch	**Control**				**rGO**				**HA**				**LDFH-CFX**			
Task	*Mean*	*SD*	*Max.*	*Min.*	*Mean*	*SD*	*Max.*	*Min.*	*Mean*	*SD*	*Max.*	*Min.*	*Mean*	*SD*	*Max.*	*Min.*
No activity	6	1	9	2	11	1	18	4	38	3	49	27	26	3	36	12
Printing 1	6	1	9	4	15	1	20	11	45	4	64	37	19	2	25	15
Printing 2	13	1	26	9	16	1	22	12	52	2	60	45	14	1	17	11
Plasma 1	10	1	13	7	14	1	18	11	47	2	51	41	16	1	19	13
Plasma 2	13	1	16	10	16	1	18	13	51	2	58	44	14	1	17	10
Cleaning	8	1	11	5	16	1	20	13	46	2	52	40	-	-	-	-
PRINTING	10	1	26	4	16	1	22	11	49	3	64	37	17	2	25	11
PLASMA	12	1	16	7	15	1	18	11	49	2	58	41	15	1	19	10