NanoTBTech

Nanoparticles-based 2D thermal bioimaging technologies

H2020-FETOPEN-1-2016-2017

Grant Agreement: 801305

Deliverable number D7.5 (D48)

Dissemination and Exploitation Plan (DEP)

First Version

Project Deliverable Information Sheet

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*This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No **801305.***

Abbreviations and Acronyms

CA	Consortium Agreement
CIBER-BBN	Consorcio Centro de Investigación Biomédica en Red de Bioingeniería, Biomateriales y Nanomedicina
CIBER-ER	Centro de Investigación Biomédica en Red de Enfermedades Raras
CIBER-ONC	Centro de Investigación Biomédica en Red Cáncer
CNRS	Centre National de la Recherche Scientifique
CSIC	Agencia Estatal Consejo Superior de Investigaciones Cientificas
DEP	Dissemination and Exploitation Plan
DoA	Description of action
EATRIS	European Infrastructure for Translational Medicine
EIC	European Innovation Council
EP	Exploitation Plan
EU	European Union
FET	Future and Emerging Technologies
FIBIRYCIS	Fundacion para la Investigacion Biomedica del Hospital Universitario Ramon Y Cajal
GA	Grant Agreement
H2020	Horizon 2020 Framework Programme
IPR	Intellectual Property Rights
NoCanTher	NoCanTher - Nanomedicine upscaling for early clinical phases of multimodal cancer therapy
SAAT	Sociétés d'Accélération du Transfert de Technologie
SME	Smalll and Medium-sized Enterprises
WP	Work Package(s)

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D7.5 DISSEMINATION AND EXPOITATION PLAN (DEP)

NanoTBTech - Nanoparticles-based 2D thermal bioimaging technologies is an European Union's Horizon2020 Programme funded project (Grant Agreement No 801305) coordinated by University of Aveiro (UAVR, Portugal). It is executed by a consortium of 9 partners, two of which SMEs: Fundacion para la Investigacion Biomedica del Hospital Universitario Ramon Y Cajal (Fibirycis, Spain), Centre National de la Recherche Scientifique (CNRS, France), Agencia Estatal Consejo Superior de Investigaciones Cientificas (CSIC, Spain), Institut Za Nuklearne Nauke Vinca (Vinca, Serbia), Instytut Niskich Temperatur I Badan Strukturalnych Im Wlodzimierza Trzebiatowskiego Polskiej Akademii Nauk (WPAS, Poland), Universiteit Utrecht (UU, The Netherlands), Nanoimmunotech SL (NIT, Spain), Biospace Lab SA (Biospace Lab, France). The project runs from September 1st 2018 and will on August 31st 2021.

The goal of NanoTBTech is to develop a 2-D thermal bioimaging technology featuring submicroscale resolution, based on nanothermometers and heater-thermometer nanostructures. Nontoxic luminescent nanostructures, operating essentially beyond 1000 nm, for in vivo nanothermometry and nanoheating, will be designed, synthetized and bio-functionalized. Furthermore, to monitor the temperature-dependent nanostructures' luminescence we will develop a novel imaging system. The effective delivery of that major advance in 2-D thermal bioimaging will be implemented through two impactful biomedical showcases: highly spatially-modulated intracellular magnetic/optical hyperthermia and in vivo detection and tracking of cancer. It is expected that in the long-term, the developed technology will have a broad impact on non-invasive clinical imaging and theranostics. Multiple conceptual breakthroughs can be further envisaged from the proposed 2D-thermal imaging system, credibly spreading its impact towards non-biomedical technological areas.

It is essential to convert public investment in R&I activities into socio-economic benefits for the society. This is reflected in the Horizon 2020 Rules for Participation, with a clear emphasis to the beneficiaries' obligations to exploit and disseminate the outcomes of the funded activities. This deliverable appears in this context, being consistent and in support with the strategy laid down on the Data Management Plan (D.7.6).

The present document – D7.5 - Dissemination and Exploitation Plan (DEP) is a deliverable of Work Package 7 (WP7) of NanoTBTech that deals with coordination and management of the project. However, all the partners are also involved in the dissemination and exploitation of outcome results of the project.

OBJECTIVE:

NanoTBTech DEP establishes a strategy to ensure an effective dissemination, technology and knowledge transfer, as well as communication and exploitation channels and activities to be carried out by the Consortium. It is, by nature, a dynamic document and, therefore, will be updated even after its formal delivery. The document is organized in 2 parts: 1) Dissemination Plan and 2) Exploitation Plan.

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1. Dissemination Plan

Dissemination is defined as the public disclosure of the results by any appropriate means, including scientific publications in any medium. A dissemination plan is an essential element of all good research practice enclosing the transfer of knowledge and results to the ones that can best make use of it. It maximizes the impact of research, enabling the value of results to be potentially wider than the original focus. It also prevents results becoming sticky and effectively lost, reinforcing and promoting the profile of the organisation[1]. Dissemination is with regards a way to communicate all results which are not restricted due to the protection of intellectual property, security rules or legitimate interests.

Planning the dissemination activities of a funded project is mandatory under the regulations of the European Union's Horizon 2020 programme. The main goal is to promote knowledge, general public awareness, education and transparency. Dissemination is also related with how communication is performed, to whom and how it will be done. The strategy to adopt should raise awareness about the social impact and exploitation potential of the project in scientific and industrial communities, and general public.

Table 1 summarizes the planned dissemination actions to be carried out during and after NanoTBTech project. These depend on the target audience and the message to be transmitted.

Table 1: Dissemination actions

ACTION	LEADING PARTNER	TARGET AUDIENCES	INDICATORS
Publications Of results in peer-reviewed journals	All	Scientific Community	Impact factor, citations, downloads
Website	UAVR	Scientific community, general public, industry/stakeholders, academia	Visitor analytics
Logo	UAVR	Scientific community, general public, industry/shareholders, academia	Logo recognition
Leaflet	UAVR	Scientific community, general public, industry/academia	Contact requests, demonstrations of interest

[1] Adapted from : http://ec.europa.eu/research/participants/portal/desktop/en/support/reference_terms.html

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Scientific Events: conferences, workshops, seminars,	UAVR; FIBIRYCIS, other partners	Scientific community, general public, industry/shareholders, academia	*Organized*: number of events organized; number of attendees, satisfaction surveys; *Attended*: number of invited talks, oral presentations and posters
General public events: open days	All	General public, academia, industry/shareholders, scientific community	*Organized*: number of events organized; number of attendees, satisfaction surveys
Social media	All	Scientific community, general public, industry/shareholders, academia	Number of followers
Press releases and public outreach (journals, radio, TV)	All	Scientific community, general public, industry/shareholders, academia	Number of appearances, number of interviews, speeches
Roll-up (s)	UAVR, other partners	Scientific community, general public, industry/shareholders, academia	Contact requests, demonstrations of interest

Table 2 presents the roadmap for dissemination actions during the project lifetime and beyond.

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Table 2: Roadmap of dissemination actions of NanoTBTech

	NanoTBTech Project			Post NanoTBTech Project		
	1st Year	2nd Year	3rd Year	4th Year	5th Year	6th year
Logo & image						
Website						
Leaflet						
Social media						
Press releases & public outreach & promotional material						
Scientific publications						
Conferences						
Events						
Related projects						

1.1. NanoTBTech logo and image

A specific logo was designed to give a visual identity to the project (Fig. 1). The logo (deliverable D7.1) was handled by WP7 (UAVR) on month 2 of the project and is systematically used in all the promotional and dissemination actions of the project, including website, presentations, posters, communications, and documents.

The logo can be downloaded directly from the website or requested by direct contact with the project manager (Eliana Cavaleiro) or WP7 leader (Rute Ferreira).

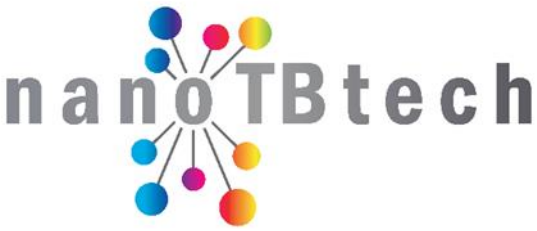

Figure 1: NanoTBTech Logo

To create a consistent style, format and an identity for the project, template files for Microsoft PowerPoint® and Microsoft Word® documents (Annex I), were created to be used in all the dissemination actions.

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Guidelines: The partners should use the templates created when presenting the project or its outcomes, in internal or external events. The files are available in the private area of NanoTBTech website or may be requested (Eliana Cavaleiro or Rute Ferreira).

1.2. Website

The dedicated NanoTBTech website (Figure 2) has been set up from the beginning of the project (D7.1, M2). The website is the main communication platform of NanoTBTech activities comprising basic information targeted to the public and specific information devoted to the different stakeholders linked to the project.

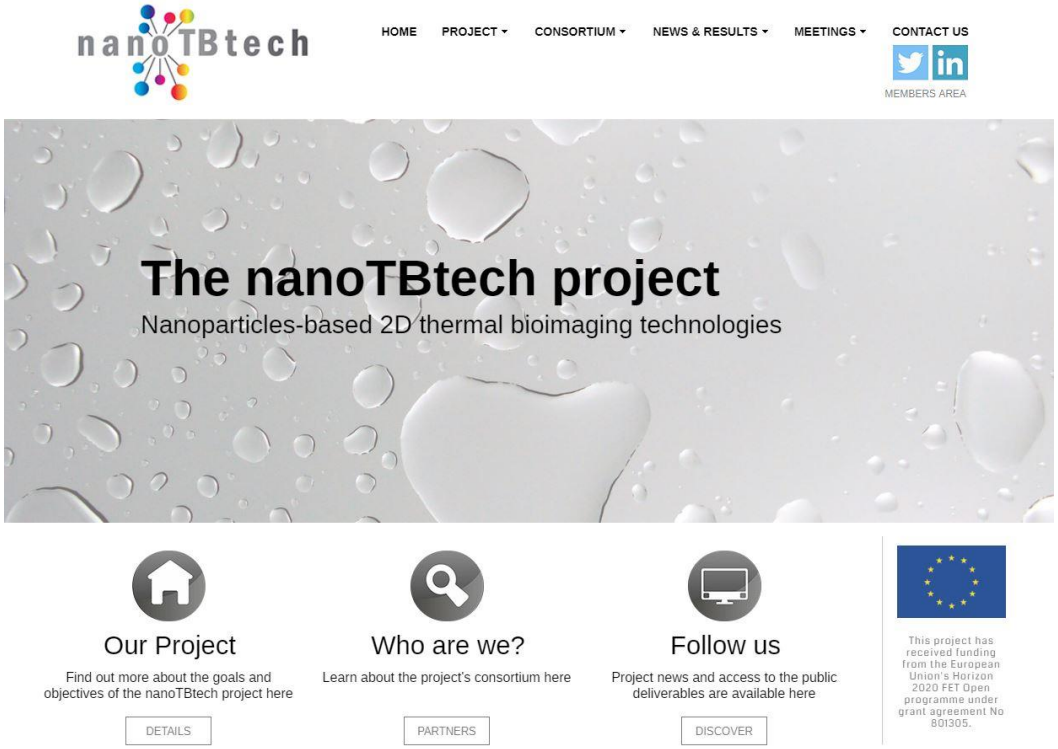

Figure 2 : Screen capture of NanoTBTech Website (http://www.nanotbtech.eu/)

The website is attractive and informative and includes a restricted area to all the Consortium Members to simplify continuous communication between partners. It was designed to reach a larger community from scientists to general public interested in luminescence, nanomaterials, and nanothermometry technologies.

Key features of the website include:

Homepage – Describes what the project is about, who are the partners and the team, and how to follow the project outcomes, displaying the Social Media (LinkedIn and Tweeter) and Members Area icons.

Project – Gives an overview of the project, objectives, work packages, and committees

Consortium – Short *CV* of NanoTBTech coordinator and WP leaders respectively.

News & Results: includes project outputs, news and calendar events, newsletter and publications related to the project and the Leaflet.

Meetings: Calendar and summary of the NanoTBTech meetings or organized events and their links respectively.

Contact: Contacts details of coordinator and project manager.

The website is hosted and managed by University of Aveiro (WP7 leader) (\\arca.ua.pt\Hosting\nanotbtech.web.ua.pt) and it is intended to be maintained for at least 3 years after the end of the project, or until the host considers it to be relevant and useful. Commercial analytic programs will be used to monitor the access to the website.

Guidelines: UAVR will manage the NanoTBTech website and update it regularly. If partners wish to upload any material (news, events, others), should contact the project manager. Partners are invited to include a link of the NanoTBTech website to their personal/institutional webpages.

1.3. Leaflet

A triplet format page (see Annex II) has been developed in the first half year of the project to be distributed among partners. It is intended to be hand out when attending to scientific conferences or fairs, events with schools, professional exhibitions and industrial activities. The leaflet is aimed to inform a wide audience about the project's objectives, implementation and expected outcomes. Concerning general public, the leaflet will increase project visibility, providing context, contacts and links to the project's website. The leaflet should be present in all the events related with the project.

Guidelines: An electronic and printed copy of the leaflet will be provided to all the partners. Partners will be responsible for distribution and dissemination on their personal and institutional network of contacts. A pdf file of leaflet will be available in restricted area of the website.

1.4. Social media

NanoTBTech is present on social media/networking via a dedicated LinkedIn group (https://www.linkedin.com/in/nanotbtech/), and Twitter (https://twitter.com/nanotbtech). The main purpose of using these social media is to reach wide visibility within scientific community, institutional and industrial sectors.

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Guidelines: All the social media accounts (LinkedIn and Twitter) have been set up by WP7, however partners are invited to share, forward or (re)tweet relevant information. The members of the Consortium are invited to contribute to these social media channels.

1.5. Press releases and public outreach

Project news will be disseminated regularly not only in project website but also using other channels, such as "Jornal Online" (online journal of University of Aveiro), other institutional journals from partners, regular newspapers or magazines, institutional blog, or other. Press releases will be properly prepared to ensure that general public, scientific or industry community are aware of the project, objectives and outcomes.

Each partner will also promote public awareness on general science emphasizing 2D thermal bioimaging technologies and their impact on society, by means of different initiatives. Examples of such initiatives are Fábrica Ciência Viva in Aveiro (http://www.ua.pt/fabrica/) or the participation on the European Researchers' Night. The crucial role of public funding to establish future technological leaderships in Europe will be also stressed in these initiatives. EATRIS infrastructure for Translational Medicine, which is supporting this application, will contribute to funding through its matchmaking activities. FIBIRYCIS has wide experience in advocacy, interacting with key stakeholders as government, patients´ and families' associations. Additionally, specialized Health communication channels, including TV, radio, press, twitter, are accessible to the clinical group.

An article (Annex III) summarizing the NanoTBTech project was published in Sci-Tech Europe magazine in March 2019 (https://www.scitecheuropa.eu/scitech-europa-quarterly-issue-30/93186/)

Guidelines: The WP7 will write the press releases related with the main events organized by the Consortium. However, partners are invited to write or share inputs to unforeseen news. After approval by the coordinator/consortium these press releases will be uploaded in website and disseminated using the chosen channels. When writing the press release, partners are committed to use specific standard content (date; eye-catching headline; logo; EU emblem; contact details for requesting more information).

1.6. Other Promotional Material

Other promotional material can be developed when needed. For instance, a Roll-Up (Annex IV) of the project was produced and will be further used in Consortium Meetings, fairs, or other events organized by the consortium.

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Guidelines: If partners considered relevant the promotion of the project through a roll-up, in fairs or markets, they can print out its own roll-up. The WP7 provide the pdf layout for a better harmony of information displaying.

1.7. Scientific publications in peer-reviewed journals

The NanoTBTech's results will be communicated to the scientific community mainly through the publication in high impact and peer-reviewed journals. The target journals will be both fundamental and applied journals in physics, chemistry, medicine, materials science and multidisciplinary areas, such as nanotechnology and nanomedicine, as well as publications with an industrial audience. The NanoTBTech Consortium will follow the GA rules on open access publications (Gold or Green). All publications will be available through the project website and will be deposited into the institutional repository of the partners' research institution and/or in Zenodo.org (an EU OpenAIRE repository.).

To date, NanoTBTEch Consortium has already published some scientific manuscripts (Annex V), it is expected that the scientific production will increase during the upcoming years of the project. Annex I will be updated accordingly.

Guidelines:

According to art. 29.4 of the GA, all publications, all communications (posters, oral presentations in conferences), and any promotional material, made by the partners on NanoTBTech scope, must acknowledge the funding contribution from EU and display the EU emblem, using the following sentence: *"This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 801305."*

If partners published any type of open documents, it also should include the following statement: "STATEMENT FOR OPEN DOCUMENTS (c) 2019 NanoTBTech Consortium: The NanoTBTech Consortium (http://www.nanotbtech.eu/) grants third parties the right to use and distribute all or parts of this document, providing that the NanoTBTech project and the document are properly referenced.

1.8. Events

A crucial dissemination action is the organization/participation in events or meetings. The NanoTBTech will organize and participate in national and international meetings (targeted both academic and industrial communities) following the updates in the field. Specialized events, such as scientific congress, workshops, training events, and general public events (e.g., Researcher's Night). This is a way to reach a specialized scientific audience, providing good opportunities for knowledge exchange between scientist, industrial exhibitors and other attendants.

The main objective of congress, workshops and training events, is knowledge dissemination among the scientific community, while general public events or industrial events are more specific to target the general public and relevant stakeholders, respectively.

Event's participation:

To date, NanoTBTech members have attended to several national and international conferences, workshops and seminars (see Annex VI).

Event's organization:

As defined in DoA , NanoTBTech consortium will organize:

- A Training School (2-days workshop): this is a dedicated training school organized by FIBIRYCIS. The main aim is to train *NanoTBTech* young scientists in the fields covered by the project. It will be open to scientists from outside the consortium to maximize dissemination. The "Training School" will be held in Madrid, Spain, from 8th to 11th January 2020 (https://eventos.uam.es/34645/speakers/three-wise-men-winter-school-on-luminescent-nanothermometry-for-biomedical-applications.html). Eminent scientists on the scientific areas of the project will be invited.
- Industrial Workshop: the industrial partners will organize a workshop in the fifth semester of the project to promote NanoTBTech results and technologies, projecting them in the context of further industrial developments.

According the GA and the CA and for the internal project management, a Steering Committee (will all WP leaders) meeting is held every six-months, mainly by videoconference to discuss current topics of the project. A Consortium's meeting is held annually, where all the partners get together to discuss results and define sstrategies to tackle the next months of the project.

Guidelines: All the partners should inform the project manager about the event attendance, sending information about their own participation.

1.9. Related projects

As described in GA (in DoA), during the project the partners will participate on EU initiatives or other EU projects (e.g., NoCanTher EU project, http://www.nocanther-project.eu) interacting with related research, promoting *NanoTBTech* results and contributing to define future research directions. Furthermore, it is expected that partners collaborate with EATRIS, CIBER-ONC, CIBER-BBN, CIBER-ER in applications to EU financed projects.

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2. Exploitation Plan

Being a FET OPEN project, NanoTBTech has a strong potential for developing new technologies that will impact society. All partners of NanoTBTech are interested in the exploitation of the project's outcomes in different manners. On one hand, research partners are more oriented to transfer knowledge and technology to interested stakeholders while on the other hand, the SME partners are strongly focused on industrialization and future commercialization of the research outcomes/results.

Exploitation means "the use of results in further research activities other than those covered by the action concerned, or in developing, creating and marketing a product or process, or in creating and providing a service, or in standardization activities"[2] and it is in this context that this document arises. In fact, the Exploitation plan (EP) is, as the dissemination one, a strategic document for project, helping the beneficiaries to lay down and summarizing the bases regarding issues like intellectual property strategy, future exploitation, exponentiation and sustainability activities namely on how the result of the project will will impact the market (s), the future developments and, if applicable and to a higher level, policy making.

In general, and as stated on GA/DoA, the exploitation strategy will be led by the Coordinator in close cooperation with the two industrial partners of the consortium (Biospace Lab and NIT) and IRYCIS. The strategy will be directed to targeted stakeholders and companies with interest in temperature sensing at the nanoscale, after IP is secured.

There are several important points to be detailed, as addressed in the following pages.

2.1. Exploitation Committee

NanoTBTech envisages the establishment of an "Exploitation Committee". It will gather people from different partners, with skills and competences relevant for this task. In concrete the Exploitation Committee will composed by:

- 1-2 Representative from each industrial partner (NIT and Biospace)
- 1-2 Representative of the Coordinator
- 1-2 Representative of the IRYCIS development office

This committee will draft and implement the actions foreseen in the EP, namely:

- IPR management
- Discussion and drafting of any licensing agreements, based on the upfront any IPR Agreement needed and in line with the regulations, procedures and interests of the different parts involved.
- Market and Business opportunities analysis, namely outlining the analysis of potential customers, competitors, environmental conditions, product weaknesses and strengthens.

[2] Adapted from : http://ec.europa.eu/research/participants/portal/desktop/en/support/reference_terms.html

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- Proper coordination with the dissemination activities and data management plan;

The committee will formally discuss exploitation issues every three months by teleconferencing. When needed, it will contact the partner's exploitation officers (to fill patents, for example) or other relevant stakeholders. The Coordinator will be the project contact point for potential industrial partners.

Furthermore, its action will include the organization of an industrial workshop to promote NanoTBTech results, discuss possible commercial exploitations and identify potential stakeholders and companies interested in 2D thermal bioimaging technologies. This is scheduled to occur in Paris at M30 of the project.

The committee will be responsible for updating the EP on a regular basis.

2.2. IPR management

Both the Grant Agreement (GA) and the Consortium Agreement (CA) include description and provisions regarding of a number of issues related to IPR, specifically:

- GA section 3 "Rights and obligations related to Background and Results"
- CA section 8 "Results";
- CA Section 9 "Access Rights";
- CA Attachment 1 "Background included"

Partners who own knowledge suitable for patenting or suitable for another protection route (e.g., trademark) will be encouraged to fill in applications for patents or adequate form of protection and shall supply details of applications to the other consortium partners.

Specific agreements (confidentiality or others) will be signed among partners and with external entities (eg. Potential licensees) whenever sensitive IP and commercial issues are detected.

Guidelines: Every partner is requested to communicate to the Exploitation Committee, as soon as possible, any exploitable foreground and any IP protection measures such as patents or trademarks. For this purpose, reporting forms will be elaborated and be available for download at the NanoTBtech private area of the website. In principle, these reports/logs should contain information on:

- Contributing Partners and identification of specific contribution/role in the development
- Identification of IPR type
- Status of IPR: Background (type and partner owner)
- Status of IPR: Foreground (type and partner owner)
- Status of IPR: Exploitation Forms (type and partner owner) e.g., direct industrial use, patenting, technology transfer, license agreement, publications, standards, etc.
- Status of IPR: Application Title
- Related Publications / Embargo end date (if applicable)

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- Related Patents (European Patent Office Esp@cenet , google patents, Thomson Innovation)
- Partner/s involved expectations
- Confidentiality (Yes/No)
- Innovativeness introduced compared to already existing Products/Services
- Unique Selling Point (competitive advantages)
- Product/Service Market Size
- Market Trends/Public Acceptance
- Product/Service Positioning Legal or normative or ethical requirements (need for authorizations, compliance to standards, norms, etc.)
- Competitors Prospects/Customers
- Cost of Implementation (before Exploitation)
- Time to market Foreseen
- Product/Service Price
- Sources of financing foreseen after the end of the project (venture capital, loans, other grants, etc.)

These logs are of uttermost importance for correct IPR management will contain vital information for invention disclosures, patent applications and agreements.

IPR management includes also analyses on the intellectual property that is needed or that will be brought to the project (e.g., knowledge and inventions) ; these analyses should also cover preliminary freedom to operate searches.

2.3. Market analysis and business opportunities

The Consortium has the capability to integrate the transfer of developed know-how, leading to the exploitation of the projects results. In fact, the consortium includes the technology providers and the technology seekers/users and it is expected that the 2 SMEs, Biospace (imaging) and Nanoimmunotech (nanotoxicity) will be the first to benefit from the project outputs (potential technology market introducers).

In order to maximize the exploitation possibilities and the valorization of the results, a market analysis and identification of business opportunities will be made by the Exploitation Committee. This will include (not exhaustive listing):

- Target market analysis (size, geographic analysis, segmentation, trends, etc.)
- early identification of potential partners/customers/users (including their needs)
- analysis of potential geographical coverage
- main competitors (technologies, products, services; and companies)
- competitive advantages

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2.4. Technology Evaluation, Roadmap and Business Model

The technology/results/project outcomes will be evaluated for their potential for innovation and their ability to reach/target the market. This will result in a technological road map to determine the shortest 'time to market' and the best strategies to accomplish successful market introduction.

Evaluation will include different steps/phases:

- Analysis of technological needs, namely on technology further development: proof of concept; lab scale verification; potential for industrial scale up.
- Time to market evaluation, based the data from the technological needs.
- Technology surveillance: based on data/requirement the technologies/results/solutions that are potentially closer to the market, will be identified

A business model will be defined based on the information, combined with the information from market analysis and business opportunities (see 2.4).

2.5. Indicators

In order to evaluate and keep tracking on the implementation of the exploitation plan/strategy the consortium proposes a set of indicators, some of which are also related to the dissemination strategy:

- number of participations to industrial events related to luminescence, nanoparticles, bioimaging, temperature measurements (meetings, workshops, fairs, etc.)
- number of participants on the industrial workshop (e.g., academics, industrials, investors)
- number of participations to training events related to exploitation of results
- number of patent requests filled
- number of start-up companies created
- number of licensing agreements
- number of IPR logs
- report(s) on market analysis and market opportunities
- report(s) on technology evaluation, roadmap and business model

2.6. Post-Project measures

The potential of NanoTBtech results does not end with the official ending of the project. It is expected that NanoTBTech's results will boost the appearance of new collaborative research projects, especially devoted to technological applications of 2D thermal imaging. It is expected that the two SMEs engaged in the consortium, together with eventual start-ups created in NanoTBTech, will play a crucial role on that aspect. In addition, the valorization of the results of the project is expected to continue in the post-period project – despite the efforts and strategy that will be made during the project's execution, it is not unlikely that the IPR processes (eg. management of submitted patents/patent requests or in terms of valorization and exploitation of those IPR - potential negotiations in order to get commercial agreements) continue after the project end In addition, for

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results that may need further development or maturation, SATT (of which CNRS is a stakeholder), may finance the maturation phase, supporting the development of prototypes and bringing them into the market. Also, future applications to EIC's FET Innovation Launchpad or to EIC Transition to Innovation Activities may be considered, in order to turn promising results from NanoTBTech into genuine technological or societal breakthrough and disruptive innovations. Other Horizon Europe instruments, other international initiatives or national initiatives of the partners' own countries may be further explored.

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3. Annexes

3.1. Annex I

Microsoft Word® (a) and Microsoft PowerPoint® (b) documents created to be used in NanoTBTech Project

NanoTBTech

Nanoparticles-based 2D thermal bioimaging technologies

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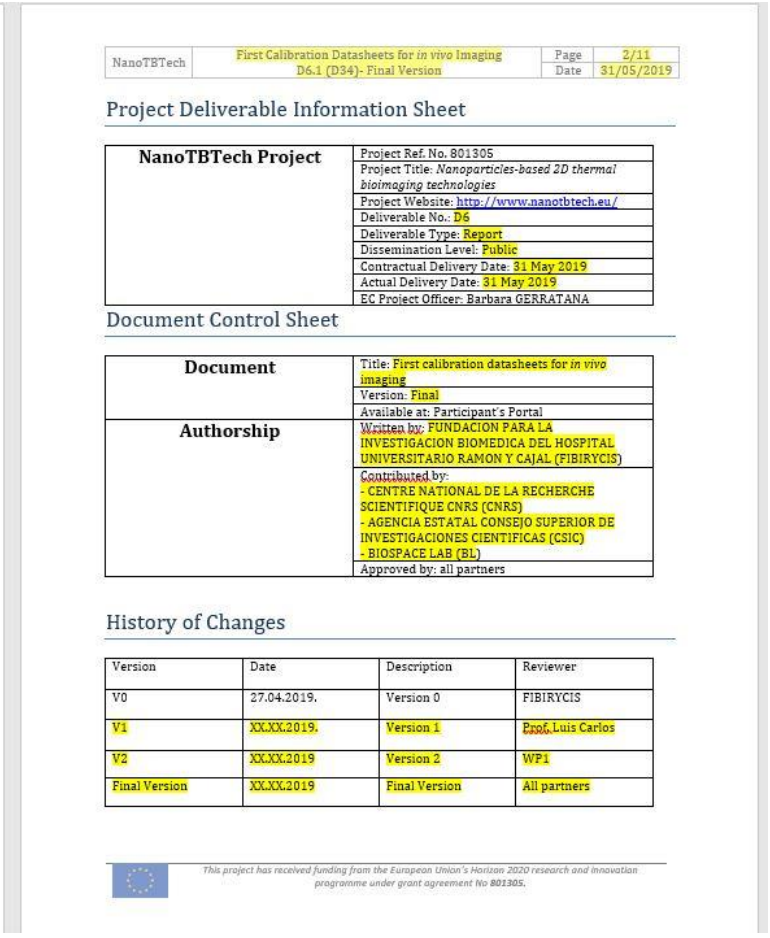

NanoTBTech | First Calibration Datasheets for *in vivo* Imaging D6.1 (D34)- Final Version | Page 2/11 | Date 31/05/2019

Project Deliverable Information Sheet

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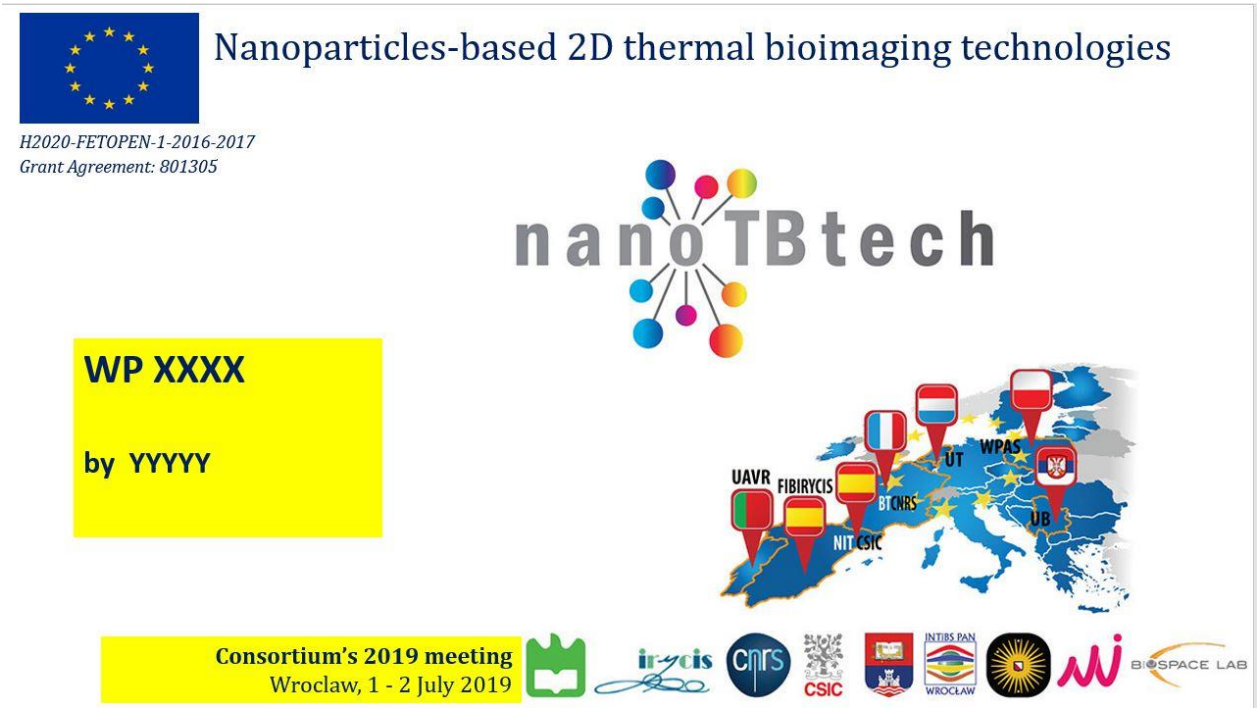
V0	27.04.2019.	Version 0	FIBIRYCIS
V1	XX.XX.2019.	Version 1	Prof. Luis Carlos
V2	XX.XX.2019	Version 2	WP1
Final Version	XX.XX.2019	Final Version	All partners

This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 801305.

a)


Nanoparticles-based 2D thermal bioimaging technologies
H2020-FETOPEN-1-2016-2017
Grant Agreement: 801305
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Wroclaw, 1 - 2 July 2019
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BIOSPACE LAB

b)

3.2. Annex II

Leaflet, deliverable D7.4 (D47), February 2019

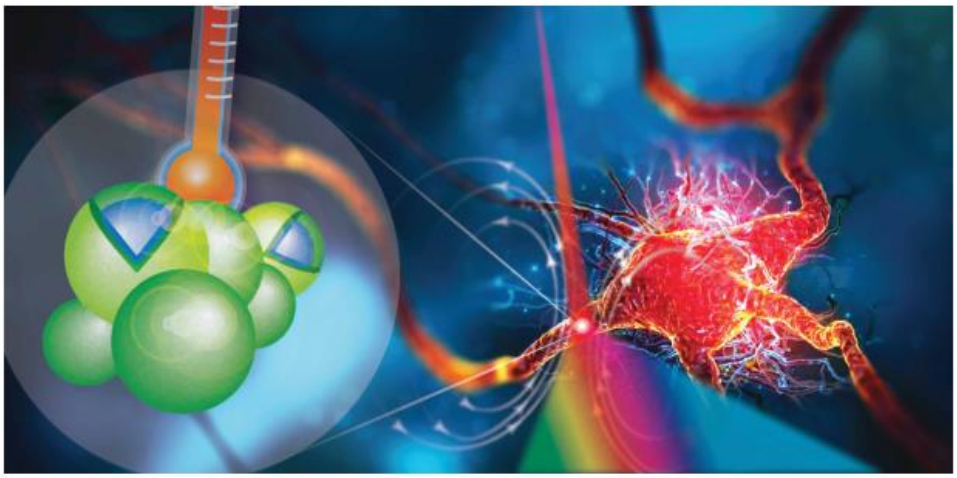
3.3. Annex III

Article published in Sci-tech Europa magazine, March 2019.

THE MEDICAL SPACE PROFILE

Nanoparticle-based 2D thermal bioimaging technologies (NanoTBTech)

The Horizon 2020 FET-OPEN-funded project NanoTBTech is leading the change towards new thermal bioimaging technologies



AT the dawn of medical science, way before the formal appearance of the scientific method, the Roman physician Celso/Celsus had already identified *calor* – the local increase of temperature – among the cardinal symptoms revealing inflammation process, (together with *rubor, tumor* and *dolor).* During the subsequent 2000 years of biomedical history, humankind has acquired further and deeper knowledge about the relationship between a great number of health disorders and anomalous temperature distributions in the affected organs. For instance, tumoural tissues have been seen to display different thermal relaxation dynamics than healthy ones.

At this point of the struggle, in order to solve key medical issues, researchers need to address several temperature-related fundamental biological issues. In living organisms, for instance, temperature is continuously fluctuating as it relates to many cellular functions, including gene expression, protein stabilisation, enzyme-ligand interactions, and enzyme activity. Moreover, the expression of heat-shock, cold-shock, and some virulence genes is co-ordinated in response to temperature changes. Intracellular temperature depends on the chemical reactions occurring inside cells, which are accompanied by either heat release or heat absorption, with the concomitant modification of the temperature.

Temperature changes and their spatial distribution are not just very relevant parameters that clinical physicians wish to accurately detect and quantify. Indeed, by purposely inducing a temperature change in a controlled local way, great healing effects can be achieved. In particular, hyperthermia is a harmless precision medicine method to kill malignant cells by thermal ablation and thermally-modulate the tumour microenvironment in order to have synergic effects with standard cancer treatments.

Currently, hyperthermia can be induced either by irradiation with a near infrared (NIR) laser or by an AC magnetic field. Indeed, magnetic hyperthermia already constitutes a reality that has received European regulatory approval for tumours' treatment as adjuvant or neoadjuvant therapy. However, the challenge is now to reach real-time thermal control over treated tissues, thus achieving a minimally invasive precision therapy with little collateral damage.

The challenge ahead: the right way to measure temperature for biomedical purposes

The use of temperature measurements for biomedical technology has a two-pronged promise to fulfil, namely the detection and spatial mapping of temperature gradients for a better and earlier

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detection of diseases, and real-time monitoring of hyperthermia treatments to avoid them causing more harm than good. To tackle those two complex issues, the key technology needs are non-contact thermometry granted with sub-micrometre resolution, providing high sensitivity thermal readout in a real-time mode (see Fig. 1).

Techniques able to go clearly below 1µm at cellular level and smaller than 1cm for *in vivo* targets are urgently needed, as the traditional contact-based sensors and mid infrared thermometers are not suitable for measurements at that tight spatial range.

Modern medicine has reached a point such that the use of traditional thermometers (e.g., liquid-filled and bimetallic thermometers, thermocouples, pyrometers, and thermistors) does not satisfy neither contactless nor submicrometric spatial resolution, that are required, for instance, to monitor the aforementioned intracellular temperature fluctuations. Although diverse biocompatible thermometers have been recently proposed, the area is still in its infancy and requires extensive and comprehensive theoretical and experimental work. Moreover, examples of *in vivo* thermal sensing are currently very scarce.

The NanoTBTech approach: a radical bet for luminescence-based nanothermometry

The main pathways (see Fig. 2) of our original approach are small size probes (luminescent nanoparticles), non-invasiveness of the methodology (NIR-to-NIR deep-tissue luminescence thermometry), and real-time readout. Thus, the planned outputs are:

- The fabrication of nontoxic, long-circulating 'stealth', functionalised, tumour-targeted and luminescent nanoparticles with high thermal sensitivity values. The temperature dependence of those nanoparticles' NIR emission spectra over time constitutes a spectroscopic fingerprint, linked to temperature changes happening around them. NanoTBTech researchers previously obtained outstanding results regarding the use of NIR-emitting nanoparticles as subcutaneous thermal probes in small animal bodies. They also applied emitting nanoparticles to unveil fundamental tissues' properties (as opposed to superficial) in *in vivo* conditions, thus evidencing the potential of NIR luminescence nanothermometry as a diagnosis tool
- Coupling luminescent 2D time-resolved thermal imaging and optical microscopy imaging under NIR irradiation (or AC magnetic field) in two different simple and compact prototypes to (a) monitor local hyperthermia in cells and (b) to study *in vivo* time-gated and 2D hyperspectral magnetic- or optically-gated thermal transient thermometry in depth tumoural models

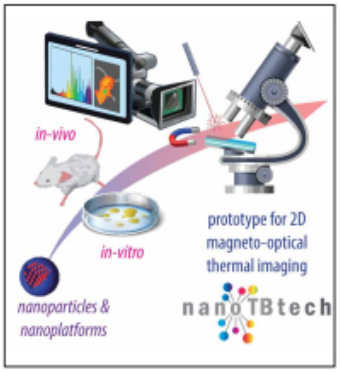
This thermal imaging modality is still less mature than many others, such as computed tomography (CT), magnetic resonance imaging (MRI) or positron emission tomography (PET), - all of them clinically applied already. However, thermal imaging based on luminescence, neither requiring long scanning times nor needing post processing analysis, provides a kind of real-time readout far from the reach of all those competing techniques.

NanoTBTech looks beyond the pure acquisition of knowledge. The effective delivery of a clean-cut breakthrough in 2-D thermal bioimaging technology will come through two impactful biomedical showcases, to demonstrate and apply the technological step forward: highly spatially-modulated intracellular magnetic/optical hyperthermia, and the *in vivo* detection and tracking of cancer.

Collective expertise to fulfil the NanoTBTech ambition

Our ambition is to develop a dedicated imaging platform with unprecedented performance leading to major advances in 2D thermal imaging technologies. Moreover, we foresee the project delivering novel insights about cell pathology and physiology, heat transfer at the nanoscale, and non-invasive detection of subcutaneous anomalies, in turn contributing to the development of novel theranostic tools. This requires a co-ordinated effort, which will not only address nanostructures' design and functionalisation but also characterisation/modelling, instrument assembling, software development, imaging interfacing, control and clinical expert inputs.

NanoTBTech brings together materials scientists, nanothermometry researchers, medical research institutes and companies devoted to nanotechnology, all of them with outstanding experience. Such a multinational consortium will supply functional technology, spreading it out through the European Research Area and to European citizens. The assembled consortium will accomplish that goal by way of moving results and discoveries captured in research papers to become prototypes that can match real life needs, first at translational centres, and tomorrow at hospitals. In the long-term, we foresee our technology as having a broad impact on non-invasive clinical imaging and theranostics.



NanoTBTech's partners

CICECO – Aveiro Institute of Materials, Universidade de Aveiro (UAVR – Portugal) is co-ordinating the project. Eight other partners participate in NanoTBTech:

- Fundacion para la Investigacion Biomedica del Hospital Universitario Ramon Y Cajal (FIBIRYCIS – Spain)
- Centre National de la Recherche Scientifique (CNRS – France)
- Agencia Estatal Consejo Superior de Investigaciones Cientificas (CSIC – Spain)
- Institut Za Nuklearne Nauke Vinca (Vinca – Serbia)
- Instytut Niskich Temperatur I Badan Strukturalnych Im. Wlodzimierza Trzebiatowskiego Polskiej Akademii Nauk (WPAS – Poland)
- Universiteit Utrecht (UU –The Netherlands)
- Nanoimmunotech SL (NIT –Spain)
- Biospace Lab Sa (Biospace Lab –France)

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3.4. Annex IV

Roll-up of the project, April 2019.

3.5. Annex V

List of scientific publications – to be update regularly in DEP and NanoTBTech Website

Partners	Title	Journal
UAVR	Lanthanide-Based Thermometers: At the Cutting-Edge of Luminescence Thermometry	Advanced Optical Materials
FIBIRYCIS	*In Vivo* Contactless Brain Nanothermometry	Advanced Functional Materials
VINCA	Li1.8Na0.2TiO3:Mn4+: The highly sensitive probe for the low-temperature lifetime-based luminescence thermometry	Optics Communications

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3.6. Annex VI

List of Posters

Partner	Title	Congress	Authors	Date	Place
VINCA	Luminescence and structural and properties of red-orange phosphor Y2Mo4O15: Eu3+ calcined at different temperatures	8th International Symposium on Optical Materials	**Jelena Papan**, Zoran Ristić, Dragana Jovanović, Aleksandar Ćirić, Miroslav D. Dramićanin,	June 9-14, 2019	Wroclaw, Poland
VINCA	Highly sensitive lifetime-based luminescence thermometry using Mn^{4+} activated $Li_{1.8}Na_{0.2}TiO_3$	8th International Symposium on Optical Materials	**Milica Sekulić**, Bojana Milićević, Vesna Đorđević, Zoran Ristić, Miroslav Dramićanin	June 9-14, 2019	Wroclaw, Poland
WPAS	Evaluation of Light-to-Heat Conversion Efficiency of Colloidal Nanoparticles	8th International Symposium on Optical Materials	**Agnieszka Paściak**, Aleksandra Pilch-Wrobel, Łukasz Marciniak, Artur Bednarkiewicz	June 9-14, 2019	Wroclaw, Poland
UU	The pathway to an optimum luminescent thermometer – Controlling Boltzmann through excited state dynamics	PRE'19, 8th International Workshop on Photoluminescence in Rare Earths: Photonic Materials and Devices	**Markus Suta** & Andries Meijerink	September 04-06, 2019	Nice, France

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List of Talks

Partner	Title	Congress	Authors	Date	Place
VINCA	Temperature dependence of Mn4+ emission: engineering of supersensitive temperature luminescence probes	8th International Symposium on Optical Materials	**Miroslav Dramicanin**	June 9-14, 2019	Wroclaw, Poland
UU	The pathway to an optimum luminescent thermometer – Controlling Boltzmann through excited state dynamics	DPC'19: 20th International Conference on Dynamic Processes in Excited States of Solids	**Markus Suta** & Andries Meijerink	August 25-30, 2019	Christchurch, New Zeland
CNRS	Towards a new nanoplatform for hyperthermia applications allowing for real-time and local temperature monitoring - Focus on nanothermometry using silver sulfide quantum dots	Nanohybrids 16	**Lise Abiven** & Corinne Chanéac	June 3-5, 2019	Porquerolles, France
FIBIRYCIS	Issues and Perspectives of NanoTBTech: Nanoparticles-based 2D Thermal Imaging	ESTE 2019: Excited States of Transitions Elements	**Erving Ximende**s & Daniel Jaque	September 09-13, 2019	Kudowa Zdroj, Poland

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UAVR	Lanthanide-Based Thermometers at the Cutting Edge of Luminescence Thermometry	9th International Conference on Rare Earth Development and Application & Annual Meeting of the Chinese Society of Rare Earths 2019	**Luís Carlos**	May 15-18, 2019	Beijing, P.R. China
UAVR	Lanthanide-based thermometers at the cutting edge of luminescence thermometry: from biomedical applications to the Internet of Things	PRE'19, 8th International Workshop on Photoluminescence in Rare Earths: Photonic Materials and Devices	**Luís Carlos**	September 04-06, 2019	Nice, France
UAVR	Luminescence Thermometry: From the Determination of the Thermal Properties of Lipid Bilayers to the Internet of Things	ESTE 2019: Excited States of Transitions Elements	**Luís Carlos**	September 09-13, 2019	Kudowa Zdroj, Poland
UAVR	Polymeric Micelles doped with Eu, Sm Complexes as a Thermometric Systems	ESTE 2019: Excited States of Transitions Elements	**Justyna Zeler,** Carlos Brites, Luís Carlos, Rafael Pinol, Angel Millán	September 09-13, 2019	Kudowa Zdroj, Poland

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3.7. Annex VII

List of NanoTBTech meetings

Meeting	Venue	Date	Partner Host
Kick-of-Meeting	Aveiro, Portugal	24-09-2018	UAVR
Consortium's 2019 Meeting	Wroclaw, Poland	1 - 2/07/2019	WPAS
Consortium's 2020 Meeting	Belgrade, Serbia	June/July 2020	VINCA

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