Knowledge translation in challenging healthcare environments: The PIOPPO experience at the National Centre of Oncological Hadrontherapy (CNAO Foundation)

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Abstract

Knowledge translation is the ability to translate concepts and ideas effectively among different stakeholders, leading to innovation and new knowledge. Translating knowledge is particularly challenging in the healthcare sector, which has been experiencing a shift from a centralized and sequential model of value creation to a more distributed and open model, where various stakeholders (including patients) act as co-creators of the outcome. According to management as well as the medical literature, knowledge translation in healthcare has been mainly seen as the translation of scientific research into clinical practice. However, different types of knowledge translation emerge, such as when multidisciplinary teams need to work together on a joint medical project. In this situation, multiple backgrounds, competencies, skills, and emotional feelings of the different stakeholders are a compelling barrier that prevents the effective transfer and sharing of knowledge. This is why knowledge translation needs a set of enablers to facilitate the transfer, sharing, and creation of new knowledge, innovation, and ideas.

This paper investigates such a perspective by analyzing the PIOPPO project from the National Centre of Oncological Hadrontherapy (CNAO Foundation) in Pavia, Italy. The CNAO is one of the few dual-beam Hadrontherapy centres in the world that provides a beam that is able to irradiate patients with protons or carbon ions to treat radioresistant tumours. The PIOPPO project is an experimental phase 2 trial involving preoperative chemotherapy and carbon ion therapy to treat resectable and borderline-resectable pancreatic adenocarcinoma.

The stakeholders involved in the PIOPPO trial have different characteristics, both in terms of competencies and emotions. The PIOPPO multidisciplinary team includes highly skilled professionals from several disciplines, which are not all related to medicine (from oncologists to physicists, from biologists to surgeons). Pancreatic cancer patients are

also involved while experiencing a challenging personal time. The paper analyses the knowledge translation flows, instruments, and issues among such different stakeholders.

Keywords: Knowledge Translation • Healthcare • Stakeholders • Multidisciplinary Teams • Medicine

1. Introduction and literature review

Knowledge translation is receiving an increasing amount of attention in academia and in several other sectors. Knowledge translation can be defined as the ability to turn 'knowledge into action, which includes "knowledge creation" and "knowledge application" to improve taking advantage of research benefits' (Graham *et al.*, 2006, p. 14). Knowledge translation is required each time the stakeholders who are involved in the process have different features in terms of skills, competencies, ages, culture, feelings, and expertise (Dal Mas, Biancuzzi, Massaro and Miceli, 2020; Lemire *et al.*, 2013; Savory, 2006; Secundo *et al.*, 2019). Such characteristics can erect barriers that prevent adequate knowledge transfer and sharing. The term 'translation' aims, thus, to be a more comprehensive concept than a simple 'transfer' (Dal Mas, Garcia-Perez, Sousa, Lopes da Costa, *et al.*, 2020; Savory, 2006).

The topic of knowledge translation in healthcare appears to be challenging. Currently, healthcare ecosystems are experiencing several massive changes related to the disruptive impact of new technologies (Dal Mas, Piccolo, *et al.*, 2019; Dal Mas, Piccolo and Ruzza, 2020; Dal Mas, Piccolo, Edvinsson, Skrap, *et al.*, 2020; Presch *et al.*, 2020) and transformation of patients' roles (Batalden *et al.*, 2016). Citizens become co-creators of their well-being, which directly affects the value of the healthcare services and products (Batalden *et al.*, 2016; Biancuzzi *et al.*, 2019, 2020; Dal Mas, Paoloni, *et al.*, 2019; Dal Mas and Paoloni, 2019). Thus, modern healthcare ecosystems engage with many different parties, including the following: patients, citizens, communities, healthcare professionals, clinical researchers, innovators, technicians, and policymakers (Dal Mas, Biancuzzi, Massaro, Barcellini, *et al.*, 2020). Such stakeholders share innovation processes incorporating knowledge flows that come from or that are co-produced with external parties, such as universities and research centres, private organizations, governmental agencies, NGOs, and public institutions (Abouei *et al.*, 2019; Cobianchi *et al.*, 2020; Dal Mas *et al.*, 2018; Gassmann *et al.*, 2010; Renaudin *et al.*, 2018).

In healthcare, one of the leading public bodies to recognize and promote knowledge translation was the Canadian Institutes of Health Research, which coined one of the first definitions that was later adopted by the World Health Organisation (Lemire *et al.*, 2013; Wallace, 2012). According to this definition, knowledge translation can be seen as 'the synthesis, exchange, and application of knowledge by relevant stakeholders to accelerate the benefits of global and local innovation in strengthening health systems and improving people's health.'[1]

The increasing relevance of knowledge translation in healthcare and medicine can be observed by conducting a literature search (Dal Mas, Garcia-Perez, Sousa, Lopes da Costa, *et al.*, 2020; Massaro *et al.*, 2016) in the primary scientific datasets. The search key 'knowledge AND translation AND healthcare OR medicine' in the title, abstract, or keywords in Scopus reveals more than 3,000 scientific contributions in several academic fields, of which over 2,000 are in the medical and clinical literature. Using the same research on PubMed, which is one of the leading clinical engines, identified more than 85,000 publications.

Most clinical papers consider knowledge translation to be the translation of scientific research into medical practice (Lemire *et al.*, 2013). However, some other novel types of knowledge translation have emerged, taking into consideration the new characteristics of the healthcare ecosystem. For example, one emerging topic investigates the knowledge translation flows from the physician (or healthcare professional) to the patient and vice versa, given the different competencies and feelings (Kerosuo, 2010). The relationships between healthcare institutions and the central government or policymakers has also been investigated (McAneney *et al.*, 2010). Effective knowledge translation is needed, for example, to transform clinical practices into new policies or to talk to the citizens and communities about health issues such as prevention (Deas *et al.*, 2013; Gibbon, 2011). Moreover, the open ecosystem and the massive impact of new technologies in medicine and surgery require interaction between researchers, technicians, and professionals who have different skills (Ardito and Messeni Petruzzelli, 2017; Straus *et al.*, 2008). Understanding how knowledge can be translated, shared, and transformed into a common outcome using various enablers and tools emerges as an original topic in the field.

Thus, this paper investigates the knowledge translation dynamics within a unique healthcare institution, the National Centre of Oncological Hadrontherapy (CNAO Foundation). The CNAO is one of the few dual-beam centres of

[1] See the link http://www.cihr-irsc.gc.ca/e/29418.html

Hadrontherapy in the world, provided with a synchrotron able to produce beam of heavy particles to irradiate radioresistant or difficult-to-cure tumors. Through the analysis of one of CNAO's ongoing experimental trials, this paper aims to answer the following research question: *What are the knowledge translation dynamics and the knowledge translation enablers that are used within a unique healthcare centre?*

2. Research method

This paper used case study methodology (Yin, 2014). Qualitative techniques 'allow researchers to discover to reveal and understand relationships between variables even within complex processes, and to illustrate the influence of the social context' (Massaro *et al.*, 2019, p. 275).

According to the literature (Yin, 2014), case studies are appropriate in the presence of a 'how' or 'why' question regarding an actual issue where the investigator has no control. Additionally, qualitative methodologies allow for a more in-depth insight into a real-world case (Ridder *et al.*, 2014) and are more understandable for practitioners (Dal Mas, Massaro, *et al.*, 2019). The next sections explain the research context, data collection, and the analysis process more in detail, to ensure transparency and reliability (Massaro *et al.*, 2019).

2.1 Research context

2.1.1 The CNAO Foundation
The CNAO Foundation is located in Pavia, in north-west Italy. The Foundation was established in 2001 with the aim of treating tumours using protons and carbon ion particles that belong to the category called 'hadrons'. The Centre, the only one of its kind because of its homemade synchrotron that produces carbon ions and protons that are optimized for cancer therapy, opened its doors to the first patients in 2011 (Cobianchi *et al.*, 2016).

The CNAO Foundation is also a renowned Research and Development Institute with a wide range of activities, from clinical and radiobiological research to translational research.

2.1.2 Hadrontherapy
Hadrontherapy represents a new frontier in radiation therapy because it uses protons and atomic ions called 'hadrons', which is from the Greek word hadrós that means 'strong', and they are subjected to a powerful nuclear force.

Hadrontherapy has several advantages (dosimetric and radiobiological) compared to traditional radiotherapy. One of these benefits is the ability to improve the dose localization, providing a high selectivity minimizing the damage to surrounding tissues. The healthy tissues benefit from the hadrons' high selectivity. Moreover, carbon ion radiotherapy (CIRT) is promising in the treatment of tumours that seem to be resistant to conventional therapy by reducing the oxygen enhancement ratio and decreasing both the capacity for sublethal repair and cell cycle-dependent radiosensitivity (Barcellini *et al.*, 2019; Facoetti *et al.*, 2019).

Among the requirements for effective application of hadrontherapy, a proton/carbon ion accelerator is needed to produce the particle beams.

Hadrontherapy is a relatively new technique in oncology, and thus, several experimental trials are ongoing in this area.

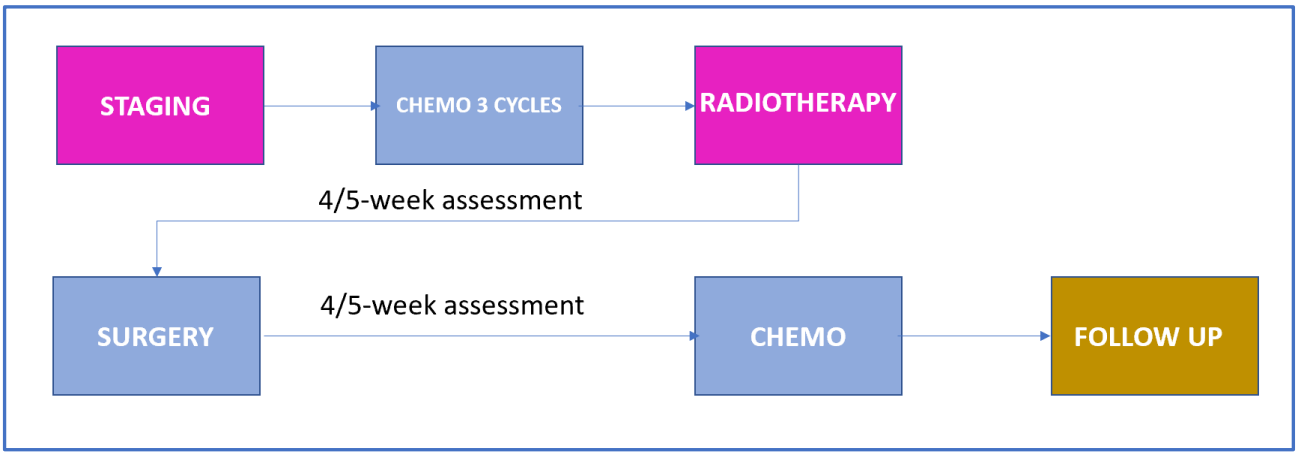
2.1.3 Current trends on pancreatic research and issues
The pancreas stands as one of the most critical human organs, and it can be affected by several diseases, among which inflammations (pancreatitis), cancer, cysts, and neuroendocrine tumors (Mayo, 2020; Rossi *et al.*, 2014). Some of such conditions can be severe, with a high mortality rate, like in the case of pancreatic adenocarcinoma. Besides all ongoing studies on pancreatic cancer, several trials involve small as well as large animals to investigate the pancreatic parenchyma. Among small animal studies, a variety of experiences emerge on islet transplantation (Pileggi *et al.*, 2006), pancreatic transplant (Merani *et al.*, 2008), and ischemic preconditions (Hogan *et al.*, 2012). Pancreatic diseases and the possible innovative cure and clinical protocols, including hadrontherapy, stand as a top priority for the scientific community.

2.1.4 The PIOPPO trial
The PIOPPO trial (Vitolo *et al.*, 2019) is investigating pancreatic adenocarcinoma, which is a severe disease that is the fourth-leading cause of cancer-related death in Europe, and it has a 5-year overall survival rate of around 5%. This

tumour can be treated only by complete surgical resection; however, up to 80% of the patients do not have such options at the time of the diagnosis because the size or location of the tumour can prevent or obstruct surgery. Previous studies conducted by the National Institute of Radiological Sciences (NIRS) in Chiba, Japan showed how carbon ion radiotherapy can be effectively used to treat locally advanced pancreatic disease. Trials have highlighted the efficacy of preoperative CIRT in reducing several obstacles (for example, the tumour size), which allows or facilitates effective surgery.

The PIOPPO trial, which was developed by the CNAO Foundation together with the General Surgery and the Oncology Departments of the IRCCS Policlinico San Matteo of Pavia, is a prospective, phase II, multicentre, single-arm study that aims to assess the efficacy and feasibility of a therapeutic protocol that combines chemotherapy, carbon ion therapy, and surgery for resectable and borderline-resectable pancreatic adenocarcinoma. Figure 1 shows the PIOPPO trial scheme (Vitolo *et al.*, 2019).

Figure 1. PIOPPO trial phases (adapted from: Vitolo *et al*., 2019, pag. 3)



2.2 Data collection and analysis

Data collection and analysis involved a variety of different stakeholders from the Institute as well as external collaborators. Professionals engaged include surgeons, radiation oncologists, medical oncologists, physicists, bioengineers, pathologists, radiologists, and radiobiologists. All the collected material was verified with the Principal Investigators of the project. Data and information were gathered from various sources to ensure their validity and to allow data triangulation (Yin, 2014). Most authors of this paper are part of the PIOPPO team. All the results were shared with, and examined by, the research team.

3. Findings

3.1. Translating knowledge at CNAO

Knowledge translation appears to be a critical issue at the CNAO Foundation. An analysis of the whole centre highlighted the presence of several types of knowledge translation.

One first-dimension concern is the need to translate scientific research into clinical practice and guidelines. As highlighted in the research context paragraph, hadrontherapy represents the latest frontier in oncology; thus, several trials are ongoing in this area. The challenge is to be able to transform such experimental tests into clinical guidelines, which have content that can be shared and applied by other centres that use protons or carbon ions. Such clinical practice should then lead to new healthcare policies. For example, decision-makers may include such approved protocols as healthcare expenses in Regions, which are paid by the government and the society. Such systems would increase the number of potential patients.

Another dimension is the multidisciplinary teams that are involved. The CNAO Foundation and its synchrotron represent a unique research and working context. Some of the employees from the centre are medical doctors or healthcare professionals, and others have a Master's degree in physics. Both competencies need to be merged to assure an effective cure. While healthcare professionals detect the tumour, decide the dose to prescribe, and the indication for the treatment, the physicists calculate the treatment plan, bioengineers, medical oncologists, surgeons, pathologists, and managers are also part of the team. Practical knowledge translation tools must be used to facilitate the work of people with such different skills and backgrounds, who share the same goal.

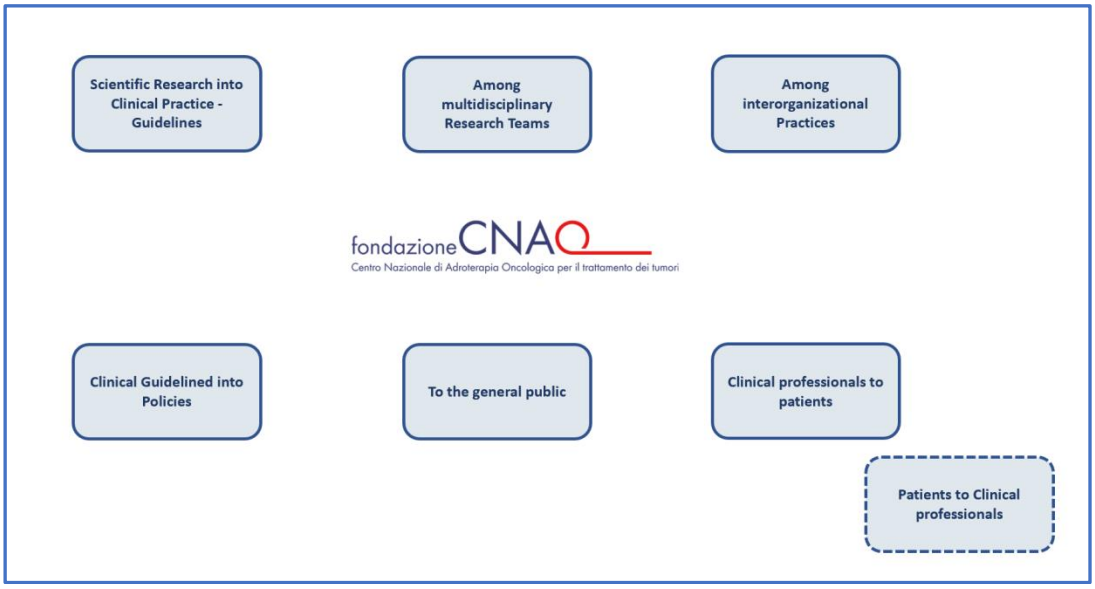
The CNAO foundation needs to cooperate with several other entities. Such organizations include the hospitals or clinics for the patients, centres that are involved that have used the protocol, and other hadrontherapy centres. Engaging with particle centres is essential to share knowledge about some specific topics or advances in research. Ongoing relationships include centres in Japan and Austria. Despite the common study and clinical ground, these centres must ensure that knowledge is effectively transferred.

Moreover, the CNAO Foundation tries to disseminate its activity and knowledge to the general public. Most people have never heard of proton or carbon ion beams as an alternative to the traditional radiotherapy. Only a few people know about the presence of a synchrotron in Pavia that is devoted to radiation oncology.

Additionally, CNAO's professionals need reach out to patients and translate knowledge to them. Decision-making is a vital task for the patient, who may need to choose among different alternatives. Sometimes, the patient may need to cooperate so actively in the treatment that the outcome may also depend on the person's will and efforts. In this case, co-production processes may emerge. Other times, patients may decide if they want to take part in experimental trials. In such cases, healthcare professionals must ensure that they correctly understand the patients' needs by helping them to translate their knowledge effectively.

Figure 2 summarises the Centre's knowledge translation roadmap.

Figure 2. Knowledge Translation Roadmap



3.2. Translating knowledge at PIOPPO

The PIOPPO trial involves professionals who belong to the CNAO Foundation as well as external team members. Several knowledge translation flows emerge when analyzing the project, its development, and the various stakeholders that are involved.

There is a need to translate knowledge among the team members. Healthcare professionals include oncology experts, biologists, and surgeons. While pathologists and radiologists make a diagnosis about the tumour, surgeons decide about the eventual operability and (medical and radiation) oncologists decide about including the patient in the trial. Physicists then calculate the treatment plan. The team members have been working together on the same topic for a while, sharing the same goal. However, there is still the need to make sure that the translation process is effective, and several tools are used. Some of the following enablers rely on technology and allow storage and sharing of knowledge: electronic medical records and online tools, image tagging, design through PowerPoint presentations, data, graphs and pictures, and using a dedicated mailing list. Other tools rely more on soft skills. Team members are encouraged to use simple language, because otherwise, people with different competencies would not understand all the information. The use of metaphors can facilitate comprehension of some unexpected issues. Kindness and the use of interpersonal skills may consolidate the team, which sets several in-person meetings and informal Question-and-Answer sessions. The long-term presence of the same people on the team represents an asset for the group. New members can learn quickly from

existing professionals. Medical and procedural tools such as up-to-date knowledge reviews and synthesis, clinical guidelines, cases, best practices, and checklists represent useful aids to facilitate the process.

Another relevant knowledge translation process concerns the relationship between the healthcare professional (oncologists or surgeon) and the patient. Knowledge translation must be adequate to ensure that the patient can make an informed decision about their eventual participation in the trial. While the physician must ensure that all the information and facts are clear, the patient must be able to communicate his or her needs and expectations. The type of disease, which is usually aggressive, leads to mixed feelings including hope, fear, and anger. Although the trial has a solid scientific base, results still need to be validated. The patients deserve effective knowledge translation to ensure that they want to participate in the study. The enablers rely primarily on soft skills. Ethics, kindness, the use of a simple language (tailored to the patient's age and education level) and metaphors, dedicated time devoted to questions, and curiosity represent the most relevant tools. Engaging with the patient's family may constitute a valid decision aid. Role-playing may be useful to understand the patient's expectations and needs. One of the surgeons declared:

Several patients ask me, what would you do if you were in my shoes?

The project mainly involves knowledge translation the general public. Dissemination activities depend on the type of audience. Citizens, industry entities, and public bodies often do not have a specific clinical background; therefore, knowledge is translated using mass media and social network channels, leaflets and brochures, and simple terminology. Testimonials from patients who underwent this treatment have been anonymously used to disseminate the trial information. Interviews have been recorded and then shared through the centre's website and its social media channels.

Dissemination activities are planned within the scientific community, to share and gather knowledge. Given the scientists' clinical background, tools include peer-reviewed open-source publications, participation in conferences and congresses, and mutual visits to other centres or hosting professionals at the CNAO Foundation. Table 1 summarises the type of knowledge translation, aims, and enablers.

Table 1. Knowledge Translation types, aims, and enablers at PIOPPO

Types of Knowledge Translation				
Among multidisciplinary Research Teams	Clinical professionals to patients	Patients to clinical professionals	To the general public (scientific community)	To the general public (citizens, private and public entities)
Stakeholders involved				
Pathologists, radiologists, surgeons, oncologists, physicists	Clinical professionals of different disciplines, patients, families		Researchers, scientists, clinical professionals	Managers, clinical professionals, citizens, public entities
Aims				
Reaching better research outcomes	Enhancing informed decision making (decision aids)		Dissemination, knowledge gathering	Dissemination, information
Enablers				
In person visit and talking	Leaflets and brochures	Engaging with the patient's family	Tours to share experiences with others	Leaflets and brochures
Clinical guidelines	Engaging with the patient's family	Use of simple language	Conferences seminars presentations	Use of simple language
Use of simple technical language	Use of simple language	Ethics	Ethics	Social and Mass Media channels
Ethics	Ethics	Use of interpersonal skills	Free access publications	Press releases

Mobile electronic Medical records and online tools	Use of interpersonal skills	Kindness	Q and A sessions	Ethics
Image tagging	Kindness	Q and A sessions	Design	Kindness
Committees and meetings	Q and A sessions	Role play	Lesson Learned and Best Practices	Press publications
Establishment of mixed teams	Role play	Dedicated time	Journal publications	Testimonials
Trainings	Dedicated time	Metaphors and examples	Clinical cases	Dedicated time
Use of interpersonal skills	Metaphors and examples		Dedicated time	Metaphors and examples
Use of evidence-based methods practice-based evidence	Checklists			
Simulations				
Short term successes making the invisible visible				
Kindness				
Q and A sessions				
Design				
Lesson Learned and Best Practices				
Clinical cases				
Discussions, debates, curiosity				
Quality assessment by stakeholders				
Self assessment				
Longevity of key actors				
Communities of practice – CoPs (mailing lists)				
Knowledge synthesis and reviews				
Dedicated time				
Metaphors and examples				
Checklists				

4. Discussion and conclusions

Analysis of the PIOPPO experimental trial that is being conducted by the CNAO Foundation highlights the presence of several knowledge translation dynamics. This includes different types of knowledge translation that emerge, once the various stakeholders are involved, and diverse outcomes are expected.

To answer our research question '*What are the knowledge translation dynamics and the knowledge translation enablers that are used within a unique healthcare centre?',* we may highlight how knowledge translation tools and enablers that vary according to the type of knowledge translation, the stakeholders that are involved, and the aims that are pursued.

More formal procedures and tools, such as knowledge synthesis and reviews, communities of practice (CoPs), checklists, and quality assessments are used among the project team members, who are highly skilled professionals from different fields.

More intangible and physiologically oriented enablers help to manage knowledge translation, sharing, and communication to and from the patients and their family. The use of interpersonal skills, role play, simple language with several metaphors, and examples can facilitate a relationship with patients who are facing a difficult time in their life, and who need to make challenging decisions. Such tools can act as decision aids.

The relationship with the scientific community is relevant to disseminate the trial results and to share practices and gather knowledge. Peer-reviewed publications, participation in medical conferences and congresses, and clinical cases emerge as the preferred tools.

Additionally, more soft-skills-related enablers help to translate knowledge for the general public are required. Design elements, video interviews, social network posts, testimonials, and press releases are among the enablers that are used to disseminate the project's details among citizens and private and public organizations.

Our study highlights how the modern healthcare system can be challenging, involving various parties who expect different outcomes in an evolving technological scenario. An effective translation process is needed to facilitate the transfer and sharing of knowledge among the stakeholders that are involved, and enablers can help with this process. However, tools must be adapted according to the type of translation that is required, the party's requirements, and the final aim that is pursued.

Similar to all studies, our research has some limitations. The case study applies to a niche sector (hadrontherapy), and its generalisability to other more traditional healthcare centres or different industries needs to be investigated. However, these limitations may be the basis for further research directions. The case study is polar, which would allow it to be transferred to other business environments.

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