SHORT REPORT

Exploring telerobotic cardiac catheter ablation in a rural community hospital: A pilot study

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Introduction

Telerobotic cardiac catheter ablation is a potentially disruptive mobile health (mHealth)[1] application that could improve access for patients living in remote areas to skilled electrophysiologists operating remotely from urban centers.[2] The lack of access for individuals living in rural regions to subspecialty surgical healthcare is a large and growing problem in need of an economically rational solution.[3–5] Further, advancements in mobile communication, internet network infrastructure, and surgical robotics are lowering the technical hurdles for implementing rural telerobotic surgical healthcare.[6,7]

While present-day surgical telementoring systems such as Odyssey (Stereotaxis, St. Louis, MO), Avail (Avail Inc, Palo Alto, CA), Proximie (Proximie, Inc, London, England), and Immertec (Tampa, FL) provide a valuable intermediary step, true single-operator telesurgery represents a substantial departure from the present-day surgical care delivery model. Since telesurgery is disruptive at multiple levels of the healthcare system, it will require addressing the concerns of a variety of different stakeholders[8]—none more critical than the surgical care team. From the perspective of workers comprising the operating room (OR) team, many questions remain unanswered regarding how the surgeon's displacement during telerobotic operations will impact the functioning of OR teams.[9] In addition, questions remain as to how best to train healthcare providers for telerobotic healthcare delivery.

To help answer these and other questions related to telerobotic specialty healthcare, we have developed a portable preclinical telerobotic catheter ablation system assembled from US Food & Drug Administration–approved/cleared products and an open-platform telerobotic data streaming service. In addition, we formed a multidisciplinary research team with experts representing clinical electrophysiology (EP), interventional radiology, sociology, computer science, engineering, robotics, healthcare economics, and cybersecurity. The purpose of this pilot research was to demonstrate a system and methods for the study of specialty telerobotic surgery in rural hospital settings.

KEYWORDS Telesurgery; Telerobotics; Cardiac catheter ablation; mHealth; Rural; Vulnerable populations (Cardiovascular Digital Health Journal 2022;3:313–319)

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Methods

The portable preclinical telerobotic cardiac catheter ablation system

The portable preclinical telerobotic cardiac catheter ablation system (Figure 1) is a telesurgery system consisting of commercial-grade EP equipment, including an endovascular robot (Amigo™; Catheter Precision, Mt. Olive, NJ). The Amigo Remote Catheter System is a steerable cardiac ablation catheter remote control system that holds and allows control of a manual cardiac ablation catheter. The Amigo Remote Catheter System allows advancement, retraction, rotation, and deflection of compatible ablation catheters. Other components include a compatible ablation catheter (IntellaNav) and an RF generator (Maestro 3000) (both Boston Scientific, Marlborough, MA), a signal display system (EP Tracer; Schwarzer Cardiotek, Heilbronn, Germany), and an electromagnetic catheter tracking system (Aurora; Northern Digital Inc, Shelburne, VT). These systems were integrated

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KEY FINDINGS

- High-fidelity simulated telesurgery coupled with ethnographic analysis has the potential to inform how we may foster the safe and effective adoption of clinical telerobotic specialty surgery by operating room (OR) teams in rural hospital settings.
- Despite the pilot nature of the study, we identified important limitations to the current setup, including an inadequate audiovisual connection between the remote operator and the rural OR staff.
- The OR staff's perceptions in this study could have been unduly influenced by the involvement of a member of the research team in the simulation scenarios. Therefore, in future studies, it may be valuable to avoid having a perceived clinical expert participate in the simulations.

into an open-platform telerobotic data streaming service and virtual reality user interface (Dopl Technologies, Inc, Seattle, WA). To represent the patient in the mock catheter ablation procedure, a portable simulated human thorax consisting of a Plexiglas case housing a 3-dimensionally printed cardiac model and simulated vasculature was fashioned, as we previously reported.[10,11]

Telerobotic simulations

Setup

All telerobotic catheter ablation simulations were performed over a single day with the remote surgeon (electrophysiologist—B.M.S.) in Chicago, Illinois, and the OR staff at Ocean Beach Hospital in Ilwaco, Washington (Figure 2). Audiovisual communication was maintained using Zoom™, a commercially available video-chat service. The remote surgeon viewed the operative field and controlled the telerobotic system using an Oculus Quest 2 and paired Oculus controllers (Oculus, Menlo Park, CA). The surgeon's virtual reality view of the operative field view, including the real-time display of the remote robotic catheter movement within the simulated patient heart, was projected on a standard computer monitor in the OR to allow the OR team to monitor the remote surgeon's actions. Simulated patient vital signs, including heart rate, blood pressure, single-lead electrocardiogram tracing, and pulse oximetry, were displayed on an Apple iPad tablet on the anesthesia tower controlled by a research team member using a simulated patient monitor application (SimMon[12]). A previously developed pericardiocentesis simulator[13] was used to allow the team to respond to the cardiac perforation challenge. In addition, 2 independent stationary laptop video cameras with audio inputs, positioned in the OR, and a GoPro (GoPro Inc, San Mateo, CA) worn by the scrub technician, filmed continuously during the simulations. Owing to COVID travel restrictions, only 2 members of the research team (R.C.J. and S.P.S.) were present at Ocean Beach Hospital. All other research team members took part in the study remotely via the Zoom portal.

Simulation protocol

All participants viewed a prerecorded presentation introducing the project and basic instructions regarding cardiac catheter ablation procedures. Four simulations, each encompassing 1 of 2 challenges, were completed over 8 hours (Table 1). To better understand the impact of remote robotic operations on operative team performance, each challenge was simulated twice: once with an in-the-room surgeon (S.P.S.) performing the mock procedure using a tethered robotic controller and once with the remote surgeon (B.M.S.) remotely performing the simulated operation using a telerobotic controller. In the latter instance, S.P.S. served as an "EP technician" in the rural OR.

Simulated procedure

All scenarios involved creating an electroanatomic map of the right atrium and simulating mapping and ablation of typical cavotricuspid isthmus atrial flutter. Draping of the "patient" was performed by the OR staff. One of the research team members (S.P.S.) simulated vascular access with assistance from the OR staff. The final setup of the robot and placement of the mapping catheter into the Amigo robot's docking station was performed by the OR staff. Only the map catheter was used in the simulations (no diagnostic catheters were placed). Because the simulations were predominantly designed to assess the OR staff's responses to the challenge events, we did not simulate intracardiac electrograms.

Challenges

The 2 challenges comprised the following: (1) loss of network connection and (2) cardiac perforation with subsequent life-threatening tamponade physiology. For telerobotic simulations, the "loss of network connection" challenge entailed abruptly (without warning) disconnecting the video chat and disabling the remote operator's ability to control the robot. In addition, the monitor displaying the operative field (electroanatomic map) was disconnected. The "loss of network connection" challenge for the in-the-room surgeon was simulated by disabling the in-the-room flat-panel display during the simulation. Participants were not made aware of the challenges prior to the simulations.

For the "Cardiac Perforation Challenge," one of the research team members slowly and progressively increased the heart rate and decreased the blood pressure displayed on the SimMon vital sign display placed on the anesthesia cart until the team responded appropriately or the scenario devolved into cardiac arrest at the discretion of the researcher (S.P.S.) overseeing the simulations. If the OR team identified the potential for perforation and pericardial effusion, a research team member (S.P.S.) performed ultrasound-guided simulated pericardiocentesis (as previously reported[13]) with the assistance of the OR team members.

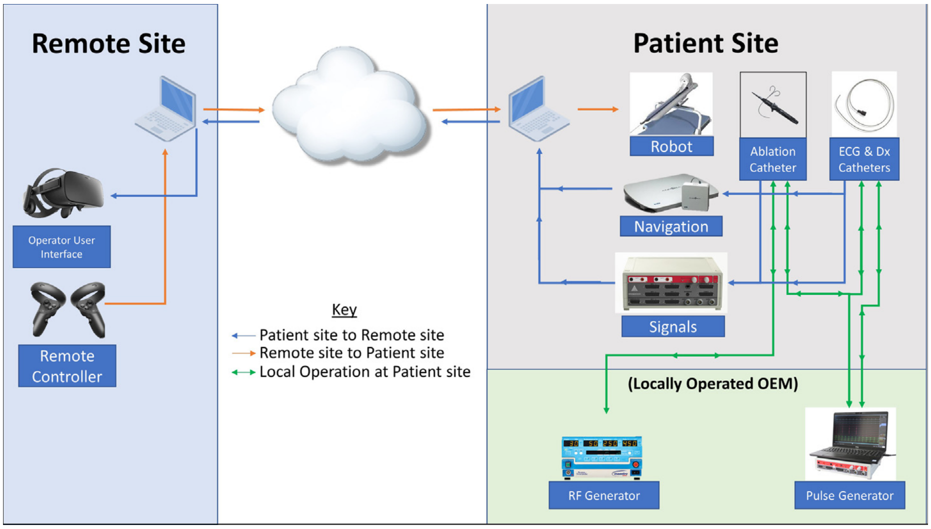

Figure 1 Schematic representation of the telerobotic cardiac catheter ablation system.

Ethnographic study of the operating room staff

Two ethnographers (L.K. and B.J.S.) observed and recorded each simulation via the OR's 2 independent stationary laptops and GoPro cameras. Cameras were positioned to capture each simulated surgery from multiple perspectives. For each simulation, the ethnographer viewed the recordings and jotted descriptive "field notes" to document verbal interactions, participant actions, and body language.[9,14]

Semi-structured interviews with participants

Twice during the study—once after the first 2 simulations and once after the second 2 simulations—the ethnographers conducted semi-structured interviews. The open-ended nature of semi-structured interviews allowed the researchers to probe for additional details or clarifications about the simulation events.[15]

Focus groups with participants

At the end of the pilot study, the ethnographers conducted a brief focus group interview with the OR team members at the Ocean Beach Hospital and Medical Center (OBHMC). They asked participants to reflect on their experience and provide additional feedback about the study.

Figure 2 Preclinical telerobotic cardiac catheter ablation in use at Ocean Beach Hospital and Medical Center operating room (Ilwaco, WA) with surgeon in Chicago, Illinois (inset).

Table 1 Simulation schedule

Time	Action
7:30–8:30 AM	In-service Ocean Beach OR team • Pre-survey • Play prerecorded introduction slide presentation Set up computer and EP equipment
8:30–9:00 AM	Break
9:00–11:00 AM	Challenge #1 simulations (local and remote surgeons)
11:00 AM–12:00 PM	Debrief & surveys
12:00–1:00 PM	Break
1:00–3:00 PM	Challenge #2 simulations (local and remote surgeons)
3:00–4:20 PM	Debrief & surveys; focus group exit interview

EP = electrophysiology; OR = operating room.

Qualitative data analysis

Data from semi-structured interviews and focus groups were transcribed using a third-party vendor (REV.com). The field notes and interview transcripts were coded using the open-access web application QCAmap.[16] In practice, this involved a first round of open coding to identify preliminary categories of interest, followed by a round of focused coding to revisit the source material to relate the categories to emerging themes.

Results

Technical outcome

The research team performed the initial equipment setup and final breakdown, but the Ocean Beach OR staff study participants completed the final preparations and sterile draping without difficulty. All components of the telerobotic system performed as intended, and the remote surgeon (B.M.S.) perceived no (unintended) latency during the simulations. However, the audio connection with the remote surgeon through a commercial video-chat portal was suboptimal (see Barriers to OR team responsiveness in following section).

Ethnographic observations

Six OBHMC OR team members—all nurses—were assigned to 1 of the 2 simulations (loss of network connection or cardiac perforation with subsequent life-threatening tamponade physiology); 1 anesthetist participated in both simulations. The self-reported sex of the OR team was uniformly female except for the anesthetist, who was male. Most OR team members had extensive experience in their roles; all but 1 had at least 5 years of experience, though not necessarily at OBHMC. The team also exhibited a high degree of familiarity; all but 3 had worked with one of the other participants for at least 5 years.

Qualitative assessment of OR team competence

The ethnographic observations and self-assessments revealed that the OR team generally responded competently and effectively to the simulation challenges, despite having no prior exposure to telesurgery or cardiac catheter ablation procedures. For instance, when asked how the team responded to the network failure incident, the anesthetist explained, "I think they reacted in a rather quick and essential manner in that troubleshooting…they were going through the right channel, checking connections, and following through in an appropriate manner, and no one was rattled. They were just doing what they should do."

Likewise, in response to the cardiac perforation simulation, the scrub technician told us: "I think different people did different things, different roles, even without being asked. Like I said, one went and grabbed the crash cart, and one focused on the ultrasound machine and prepping that and turning it on…And then, just because of working with each other so long, we can nonverbally communicate. I can just look or point to something, they grab it, no words, and it's just what I needed."

Finally, several OR team members credited the team's success to effective teamwork and their extensive experience working together—initial conditions that are likely to be found in many rural hospital settings.

Barriers to OR team responsiveness

Our analysis also revealed significant deficits in our telesurgery methods. Most notably, the noise made by the surgical robot when in operation and concomitant issues with the audio connection between the remote surgeon and the OR team made it difficult for many OR team members to respond effectively. Indeed, nearly all our interviewees mentioned struggling to hear or be heard by the remote surgeon. For example, another circulator nurse said, "It was…difficult to hear [the remote surgeon], but I think that's more of just technical difficulties. There was an echo, and we had to repeat back a few things to him." Similarly, when asked to compare the remote surgery experience with in-person surgeries, the anesthetist told us: "When he was doing the remote [surgery] and called for the ablation, and the ablation machine was making the noise, and he couldn't hear it, he didn't know if we were actually doing it at the time or not." Indeed, the ethnographer's field notes contained numerous instances when information between the OR team and the remote surgeon had to be repeated.

Second, some participants found it difficult to follow what was happening during the procedure. As a circulator nurse explained: "Generally speaking, it was hard to keep track of what was going on in regards to the machine doing the work as opposed to watching the surgeon move…In a situation when the surgeon's present, you can get a feel for what's next and how the flow is going. But as the machine was moving…it was hard to feel the flow of what it would feel like with a machine doing it, as opposed to just watching the surgeon do what he's doing."

Third, some participants reported being less able to rely on nonverbal cues to communicate with or respond to the remote surgeon. In response, some OR team members resorted to being more direct and even violated communication norms when interacting with the remote surgeon. As the anesthetist noted, "You have to override his voice and get his attention."

Fourth, some interviewees found it difficult to trust a surgeon they had never met and could not see. For instance, in response to the interviewer's question about what, if anything, changed or felt different because the operating surgeon was absent from the room, one nurse responded: "The trust factor. I've only worked with surgeons that I've known or worked with for a while and know them as a person. And so, not knowing them, trusting their skills, never having seen them do this procedure before, yeah, that was different. Out of our control." Similarly, a circulator nurse commented: "When you see someone in person or even if you saw him on the screen, you get a sense, I believe, of confidence and the ability of communication between the 2 teams. When there's a lag, as an example, you have to learn what that cadence is. If there is a lag in communication or the speech coming across, then you just have to learn what that is in order to develop a rapport really quick because that's what you have to do."

Finally, the study participants tended to treat the EP technician—who was also a member of the research team—as the authority in the room. The researcher's presence in the simulations may have reduced the communication between the team and the remote surgeon and potentially reduced the remote surgeon's authority. For instance, a scrub technician commented, "I guess even when he was the EP tech, I would look to him as the specialist like the surgeon, knowing what to do next and look to him for the leadership. I felt like…he would still be the leader…knowing the equipment and what to do next."

Study participants' concerns and considerations

During and after the study, the participants brought up several issues related to telesurgery that they believed were important to consider before moving from research to practice.

First, several interviewees worried that rural hospitals might lack the capacity to adequately handle emergencies like the one they encountered during the cardiac perforation simulation. As the circulator nurse told us, "I think just being so remote and not having the additional support, either medically, equipment wise, being so far away, and also in regards to how many people that we have on staff, and in sharing the emergency with the emergency room...it's a little scary to think about having something that is so important and so technical [be] remotely isolated."

The issue of emergency patient transport came up repeatedly during our study. For example, during the first "timeout," the anesthetist suggested checking weather conditions because inclement weather was known to delay Life Flight transports, an air ambulance service used to transport patients to urban medical centers. A focus group participant elaborated: "And even our local EMS crews, sometimes it can take us an hour or 2 to get a critical patient out because crews aren't available even out of our emergency room. So, making sure those things are set up ahead of time would definitely have to be part of the equation."

Second, some participants were preoccupied with the possibility of cybersecurity threats. Some worried that the robot could be "hacked," while others worried about bad actors assuming the role of remote surgeons. Indeed, during one simulation, the remote surgeon was unable to provide the OR team with the appropriate patient identification code. This incident later prompted a circulator nurse who participated in this simulation to say, "I think the security issue was a good a-ha moment. How do we establish security in order to identify that you are the guy that we're supposed to be working with today? That was a good thing. That was a learning point."

Finally, respondents were nearly unanimous in believing that they could adapt to the local delivery of telesurgical care with the proper training, checklists, and emergency procedures. For example, after the network failure scenario, the scrub technician told us, "You could have a list of things that you could do if that situation arose, and you can learn from it as you do it. And if other things arise, you can just add to it. And then everybody in the room will know immediately what to do in certain situations." Similarly, the circulator nurse who participated in the cardiac perforation simulation told us, "You always want to know what the next step is going to be, and until you get a sense of what those next steps are going to be, you're pretty uncertain about how to proceed or what options you might have to have in mind, or what supplies are ready to go."

Discussion

The main product of this pilot study is the demonstration of a valid system and methodology to research specialty telerobotic surgery in a rural hospital OR setting. In addition, the application of this research tool will add to our knowledge regarding the future work of telerobotic surgery in terms of OR team dynamics and the impact of network performance, cybersecurity, training, and emergency planning.

Notably, the study demonstrated that an experienced rural OR team with no prior catheter ablation or telesurgery experience could function in an effective and coordinated manner during the telesurgery simulations. Furthermore, even during the challenge scenarios—a loss of internet connectivity and life-threatening cardiac perforation—the researchers observed that the team was relatively unfazed and able to respond effectively with some guidance from S.P.S., a member of the research team who functioned as an EP technician.

The study revealed unanticipated challenges that future simulation studies will need to address during the planning phase. For instance, researchers can equip participants with better audio/visual aids in the OR to address a common concern raised during our simulations. These audio/visual aids could take the form of audio headsets and large screen displays. Another option could be optical see-through augmented reality headsets that provide audio and allow hologram visualization of the surgeon and operative field. This could both address situational awareness for the OR team and create a feeling of proximity between the surgeon and the OR staff. In addition, trust between the OR team and the remote surgeon might be fostered by incorporating more opportunities to interact with the surgeon during the "timeout" or other aspects of the preoperative setup. Finally, researchers should consider how best to integrate research team members into future simulations. For example, the use of one of the researchers (S.P.S.) as an "EP technician" during the telesurgery simulations may have led to an over-reliance on his expertise during challenge scenarios and minimized the perceived role of the remote surgeon.

Participants in our study provided valuable feedback, some unsolicited, suggesting possible elements that can be incorporated into more complex simulation designs. For instance, participants were rightly worried about how well equipped their hospital was to deal with the additional burden of telesurgery-related emergencies. The hospital's remoteness and lack of staff and resources suggest that future research should examine how to mitigate these limitations. One possibility frequently offered by the participants is to begin the study with a more formal training experience. Participants also expressed a desire for standard checklists that instruct them on how best to respond to unexpected events, not unlike the safety checklists that have become a mainstay of conventional OR procedures.

Although introducing this new form of healthcare delivery raises appropriate concerns about safety and adjustments to OR team member roles, all interviewees appeared optimistic about the future possibility of implementing telesurgery procedures in rural settings. It was not uncommon to hear comments like "I think it's up and coming, of course, and I think it would really be invaluable in the rural areas" and "I think it's a great thing to provide [to a] rural hospital like us."

Limitations

This single-center pilot study provides evidence that studying OR teams in the manner presented is feasible and valuable in iteratively developing educational content and strategies to ensure proper training of the OR team prior to clinical implementation. Owing to its small sample size and qualitative nature, however, we have been careful not to draw conclusions from observations and interviews with the OR team. In addition, our approach was narrowly focused on the perspective of the rural hospital OR team. However, the views of numerous other stakeholders will need to be explored en route to mainstream adoption of telesurgical procedures, including HIPAA compliance, cybersecurity, state licensure, liability, hospital privileging, reimbursement models, and patient adoption—to name a few.[8]

Conclusion

In the 16 years since Dr Carlo Pappone performed the first transatlantic telesurgical atrial fibrillation ablation,[17] we have witnessed a remarkable maturation of the internet and advances in surgical robotics. As a result, the challenges to widespread implementation of telesurgery are no longer technical but rather logistical and clinical. We have assembled a research team and a portable telesurgery system and incorporated ethnographic methods to better understand and mitigate these issues. We believe this study provides compelling evidence that simulated telesurgery coupled with ethnographic analysis has the potential to inform how we might foster the safe and effective adoption of clinical telerobotic specialty surgery in rural hospital settings.

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Disclosures

Stephen P. Seslar and Ryan C. James have leadership roles and equity stakes in Dopl Technologies, Inc, a for-profit company dedicated to building technology solutions for telesurgical healthcare. Dr James has also applied for patents in conjunction with instruments used in this study. The research team was loaned equipment from third-party manufacturers for this study. This study was funded by a grant from the National Science Foundation.

Authorship

All authors attest they meet the current ICMJE criteria for authorship.

Ethics Statement

The authors designed the study and gathered and analyzed the data according to the Helsinki Declaration guidelines on human research. The research protocol was deemed exempt from institutional review board oversight.

References

1. Istepanian RSH, Jovanov E, Zhang YT. Introduction to the special section on m-Health: beyond seamless mobility and global wireless health-care connectivity. IEEE Trans Inf Technol Biomed 2004;8:405–414.
2. Varma N, Cygankiewicz I, Turakhia MP, et al. 2021 ISHNE/HRS/EHRA/APHRS collaborative statement on mHealth in arrhythmia management: digital medical tools for heart rhythm professionals [Internet]. Cardiovasc Digit Health J 2021;2:4–54.
3. Cohen C, Baird M, Koirola N, Kandrack R, Martsolf G. The surgical and anesthesia workforce and provision of surgical services in rural communities: a mixed-methods examination. J Rural Health 2021;37:45–56.
4. Engelgau MM, Narayan KMV, Ezzati M, et al. Implementation research to address the United States health disadvantage: report of a National Heart, Lung, and Blood Institute workshop. Glob Heart 2018;13:65–72.
5. Skoufalos A, Clarke JL, Ellis DR, Shepard VL, Rula EY. Rural aging in America: Proceedings of the 2017 Connectivity Summit. Popul Health Manag 2017;20. S-1–S-10.
6. Cazac C, Radu G. Telesurgery–an efficient interdisciplinary approach used to improve the health care system. J Med Life 2014;7:137–141.

7. Choi PJ, Oskouian RJ, Tubbs RS. Telesurgery: past, present, and future. Cureus 2018;10:1–5.
8. Hansen RN, Saour BM, Serafini B, et al. Opportunities and barriers to rural telerobotic surgical health care in 2021: report and research agenda from a stakeholder workshop. Telemed e-Health 2021;1–8.
9. Pelikan HRM, Cheatle A, Jung MF, Jackson SJ. Operating at a distance - how a teleoperated surgical robot reconfigures teamwork in the operating room. Proc ACM Hum-Comput Interact 2018;2:1–28.
10. James RC, Monsky WL, Jorgensen NW, Seslar SP. Virtual-reality guided versus fluoroscopy-guided transseptal puncture in a cardiac phantom. J Invasive Cardiol 2020;32:76–81.
11. Seslar SP, Patton KK. Initial experience with a novel electrophysiology mapping simulator. Pacing Clin Electrophysiol 2018;41:197–202.
12. SimMon. SimMon Medical Simulation App. https://simmon-app.com/#home. Accessed July 29, 2021.
13. Tsai SL, Seslar SP. Initial experience with a novel pericardiocentesis training simulator incorporating a three-dimensional printed cardiac model. J Innov Card Rhythm Manag 2021;12:4551–4555.
14. Abelsson A, Gustafsson M, Petersèn C, Knutsson S. Physical stress triggers in simulated emergency care situations. Nurs Open 2021;8:156–162.
15. Ziewacz JE, Arriaga AF, Bader AM, et al. Crisis checklists for the operating room: development and pilot testing. J Am Coll Surg 2011; 213:212–217.e10.
16. Mayring P, Fenzl T. Qualitative Content Analysis Program QCAmap – an open access text analysis software, 15th Bienn EARLI Conf Res Learn Instr [Internet] Munich, 2013 [cited 2022 May 24], https://www.qcamap.org/ui/en/home. Accessed November 11, 2022.
17. Riordan MO. Hello Milan! Doctor in Boston performs AF ablation live via satellite on patient in Italy. Medscape. May 2006;19. https://www.medscape.com/viewarticle/788471. Accessed November 11, 2022.