# Online Remote Monitoring of Patients with Differentiated Thyroid Carcinomas and Neuroendocrine Tumors Treated with High Doses of Radionuclides

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#### Abstract

Background: Telemedicine could be very useful for patients in remote areas experiencing adverse drug reactions or being in need of sophisticated diagnostic or therapeutic procedures. The aim of this article is to show the experience of our Department of Nuclear Medicine (DNM) in telemonitoring patients with differentiated thyroid carcinomas and neuroendocrine tumors. Subjects and Methods: The DNM at the Clinical Center Kragujevac, Serbia, uses continuous remote monitoring of patients' vital functions, including heart rate, electrocardiogram, respiration rate, blood pressure, and oxygen saturation, as well as video surveillance of the physical isolation area for patients with neuroendocrine tumors (NETs) and some patients with differentiated thyroid carcinomas (DTCs), during administration of radionuclide therapy and for the days following treatment. Results: The DNM used a telemonitoring system for 156 patients with either DTC or NET who received radionuclide therapy during the last 3 years. There were 32 interventions on patients in the physical isolation area based on changes of the patients' vital functions detected by the telemonitoring system. Twenty-five patients (78%) experienced symptoms, whereas the other seven patients (22%) were symptomless. A responsible physician intervened with treatment of tachycardia (18 cases), hypertension (10 cases), hypotension (2 cases), ventricular extrasystoles (1 case), and ST-segment depression (1 case). After administration of the treatment the health status of the patients was normalized. Conclusion: From our experience gained over the past 3 years, this model of organization and supervision with a telemonitoring system of patients receiving radionuclide therapy ensures a high level of safety for the patient, with significant reduction of staff costs.

Key words: telemedicine, radionuclide therapy, patient monitoring

## Introduction

elemedicine (TM) could be very useful for patients in remote areas experiencing adverse drug reactions or being in need of sophisticated diagnostic or therapeutic procedures. It becomes vital in emergencies, when complex decisions have to be made quickly. The majority of TM systems in intensive care units (ICUs) are designed specifically for cardiovascular patients,<sup>1-6</sup> and some are oriented towards patients with malignancies.<sup>7-9</sup> In these cases, online monitoring of their physiological functions could improve care and speed recovery.

Remote patient monitoring could be achieved by specialized communication lines and equipment, but also by common Internet connections with standard equipment.<sup>1-4,10-18</sup> There is an increasing trend to use telemedical systems based on standard public tele-communication lines. Recently, systems that utilize Internet connections and new-generation mobile phones (smartphones) have become popular, because of their simplicity, low cost, and easy access.<sup>4,6,13,17,19</sup>

TM could be useful also for patients with special accommodation requirements, like those receiving high-dose radionuclide therapy of differentiated thyroid carcinomas (DTCs) and neuroendocrine tumors (NETs). After administration of a radiopharmaceutical the patient has to be accommodated in a physical isolation area for a few days, until radioactivity drops below a certain limit.<sup>20</sup>

There are legal requirements for maximal allowed radioactivity at the moment of the patient discharge from the hospital. The requirements vary among different states. For example, after administration of <sup>131</sup>I in some countries patients are allowed to live at home with 1,110 MBq,<sup>21,22</sup> whereas in Serbia maximal allowed radioactivity for outpatients is 400 MBq.<sup>23</sup> Except in the case of an emergency, during the period of isolation, contacts between patients and medical personnel are limited, in order to prevent endangering the health of the staff. This practically means that during their stay in the physical isolation area the patients are alone, which makes permanent video surveillance necessary.<sup>8</sup> Besides, the patients treated by radionuclides often have comorbidities, like coronary artery disease and hypertension, and in the case of NETs and some DTCs, there are potentially serious complications caused by biologically active tumor products (thyroxine, serotonin, epinephrine, etc.). For such patients not only video surveillance of the physical isolation area but also remote monitoring of their vital functions is necessary for timely recognition and treatment of complications. Development and implementation of remote video surveillance of the physical isolation area and the remote patient monitoring systems are increasingly

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becoming unavoidable prerequisites for nuclear medicine departments engaged in radionuclide therapy.

The aim of this article is to show the experience of our Department of Nuclear Medicine (DNM) with telemonitoring patients with DTC and NETs.

### **Subjects and Methods**

The DNM, Clinical Center Kragujevac, Kragujevac, Serbia, uses continuous remote monitoring of patients' vital functions, including heart rate, electrocardiogram, respiratory rate, blood pressure, and oxygen saturation, as well as video surveillance of the physically isolated area for patients with NETs and some patients with DTCs, during administration of radionuclide therapy and for the following few days. Video surveillance of the physical isolation area is conducted by IP cameras (Vivotek model IP7135) set either at computer view (resolution  $640 \times 480$ / color with maximal frame rate of 25 frames per second) or at mobile phone view (resolution  $176 \times 144$ /color with maximal frame rate of 5 frames per second). Remote monitoring of vital functions is conducted by a Nihon Kohden Bedside Patient Monitor (model BSM-2351) equipped with a QI-101P network card for connecting to the local area network (LAN) and a QP-985P Remote Viewer Terminal (NetKonnect-LT software) for displaying chosen wave and vital sign patterns. Using the LAN

connection, a physician from the DNM can watch at his or her personal computer (with installed NetKonnekt-LT software) the wave and vital signs pattern from the bedside monitor of his or her preference, as well as the setting of the physical isolation area filmed by surveillance cameras (*Fig. 1*). The physician's personal computer is connected through a switch to a router that is on static (i.e., globally routable unicast IP address), providing remote connections through the Internet (*Fig. 2*). Remote connection is established in the first step to this router using a virtual private network (VPN) by means of the point-to-point tunneling protocol, which is part of the Windows operating system. The second step is connection to the desktop of a computer with installed NetKonnekt-LT software, in one of the following ways:

- by remote desktop connection (RDC), which is also part of the Windows operating system)
- by virtual network computing (VNC). For this type of connection the software Ultra VNC Server and Viewer version 1.0.8.2, which is freely available on the Internet, was used.

The remote connections to the physician's personal computer with installed NetKonnekt-LT software could be made either with some other computer at the DNM (*Fig. 3*) or with the physician's home computer (*Fig. 4*) (i.e., with any computer connected to the Internet). These connections could also be established with recent models of "smart" mobile phones (*Fig. 5*). Both computers and mobile phones should have the remote connection option (i.e., suitable software support [VPN, RDC, and/or VNC]). In this way wave and vital signs



**Fig. 1.** Live video from the surveillance camera using a Vivotek monitor and signals from the Nihon Kohden BSM-2351 Bedside Patient Monitor using NetKonnect-LT software on the desktop computer in the doctor's office (1 gigabits per second [Gbps] local area network connection).

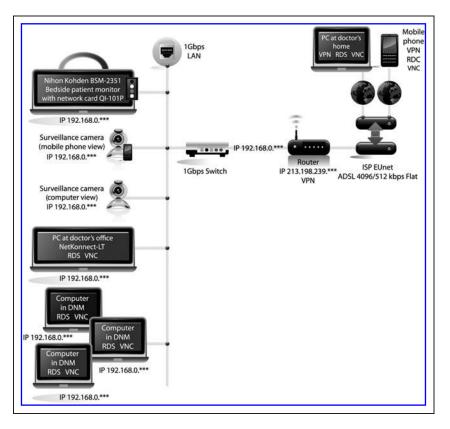
patterns could be viewed at the remote computer as well as videogenerated by surveillance cameras from the desktop of the computer running the model QP-985P Remote Viewer Terminal (NetKonnect-LT software). The video signal from the surveillance cameras could be viewed at a remote computer also directly through a Web browser, connecting to the IP addresses of the cameras.

We used the Internet connection to the Internet Service Provider (ISP) EUnet Serbia as an asymmetric digital subscriber line, with a speed of 4,096/512 kilobits per second (Kbps); such a connection provided satisfactory quality of transmission of both live videos from surveillance cameras and chosen wave and vital sign patterns from bedside monitors through the desktop of the computer running the model QP-985P Remote Viewer Terminal (NetKonnect-LT software). The signal lag was 2.1–2.8 s after the surveillance video and 1.2–1.5 s after vital sign patterns and waves from the desktop, which does not affect quality of the monitoring process. Within the LAN (i.e., within the DNM), the lag is extremely small, thanks to the transmission speed of 1 gigabits per second (Gbps).

The connection is login- and password-protected for each type of remote connections, and the firewall is set at both the router (towards the ISP) and computers within the LAN (*Fig. 2*).

#### Results

The DNM in the Clinical Center Kragujevac used the telemonitoring system for 156 patients with either DTCs or NETs who received radionuclide therapy during the last 3 years. There were 32 interventions on patients in the physical isolation area based on



**Fig. 2.** Realization of the system for remote monitoring in the Department of Nuclear Medicine (DNM). ADSL, asymmetric digital subscriber line; kbps, kilobits per second; LAN, local area network; RDC, remote desktop connection; RDS, remote desktop services; VNC, virtual network computing; VPN, virtual private network.



**Fig. 3.** Live video from surveillance camera and signals from the Nihon Kohden model BSM-2351 Bedside Patient Monitor on one of the desktop computers in the DNM (using the VNC connection on 1 Gbps LAN).

changes of the patients' vital functions detected by the telemonitoring system. Twenty-five patients (78%) experienced symptoms, whereas the other seven patients (22%) were symptomless. A responsible physician intervened with treatment for tachycardia (18 cases), hypertension (10 cases), hypotension (2 cases), ventricular extrasystoles (1 case), and ST-segment depression (1 case). After administration of the treatment the health status of the patients was normalized.

#### Discussion

The usefulness of telemonitoring has been proven for various purposes: Monitoring intraocular pressure in patients with open angle glaucoma,<sup>24</sup> blood pressure monitoring,<sup>25,26</sup> monitoring patients with asthma and chronic obstructive pulmonary disease<sup>27,28</sup> and with other severe respiratory diseases,<sup>29</sup> monitoring patients with nasal obstruction,<sup>18</sup> monitoring oral anticoagulation therapy,<sup>30</sup> etc. Telemonitoring has been used most frequently in cardiology, and many studies have proved its efficacy.<sup>1-6,31</sup> Economic consequences of telemonitoring are worthy of mentioning because reduction of total treatment costs was observed.<sup>18,29</sup> With radionuclide therapy, telemonitoring is useful because of specific requirements for accommodating patients in physical isolation areas, where it is difficult to monitor their health status<sup>8</sup> or to follow changes in radioactivity level within their bodies.<sup>9</sup> Mohr<sup>32</sup> and Wysocki et al.<sup>33</sup> presented a wide and detailed overview of different ways of implementing TM in oncology, whereas Liakhouski et al.<sup>34</sup> presented the results of their research on development and use of telemedical systems for

> teleconsultation and image analysis in patients with radiation-induced cancer. However, neither they nor other authors have taken into consideration the possibilities of vital function telemonitoring in patients with DTCs or NETs, who had been treated with large doses of radionuclides.

> Apart from the model QP-985P Remote Viewer Terminal (NetKonnect-LT software), there is also a model QP-983P Remote Viewer Server Program (NetKonnect software) on the market from the same manufacturer (Nihon Kohden), which provides for connecting many patient monitors to a hospital network and for access to data from any personal computer within the hospital network or from outer computers by VPN using the Internet. However, because the DNM already had model OP-985P Remote Viewer Terminals (NetKonnect-LT software)

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**Fig. 4.** Live video from surveillance camera and signal from the Nihon Kohden model BSM-2351 Bedside Patient Monitor on the laptop computer at the doctor's home (using VPN and VNC connections on an ASDL of 4,096/512 kbps).

installed, we decided to use this version of software for remote monitoring in order to avoid additional expenses.

Ever since the 1990s the incidence of thyroid cancer has been increasing to various extents, depending on the geographical region. For instance, based the National Cancer Institute data, the age-adjusted incidence rate of thyroid carcinoma diagnosed in 2004–2008 in the United States is about 11.0 cases per 100,000 men and women per year (based on November 2010 Surveillance Epidemiology and End Results [SEER] data submission posted to the SEER Web site).<sup>35</sup>

In Serbia, the incidence rate is somewhat lower and amounts to 6.6 cases per 100,000 men and women per year, which means that 480 new cases are diagnosed every year.<sup>36</sup> The majority of cases (over 80%) are histological types of DTC or follicular cell-derived thyroid carcinoma, which include the following histological types: papillary, follicular, and Hurtle cell carcinoma. All of these tumors share an important characteristic—a preserver NaI symporter in their cells, which is a prerequisite for them to be treated with high doses of radioiodine <sup>131</sup>I. With the exception of newly diagnosed patients, this type of therapy sometimes has to be repeated if patients have a recurrent/relapsing tumor, or metastases. This means that 500–550 therapeutic doses of radioiodine are applied yearly in Serbia.

As for NETs, their incidence is 2.5–5 per 100,000 men and women per year, which in the case of Serbia amounts to several dozens of newly discovered tumors a year. The majority of these tumors have expressed somatostatin receptors, which is a prerequisite for somatostatin analog radiopharmaceuticals therapy. Because of that, we usually use some of DOTA (1,4,7,10-tetraazacyclododecane-1,4,7,10tetraacetic acid) derivates, labeled with high doses of the appropriate radionuclides (<sup>90</sup>Y and <sup>177</sup>Lu) to be applied as therapy. Because of the specific mechanism by which these radiopharmaceuticals are bound to tumor cells, this therapy has been dubbed peptide receptor radiopharmaceutical therapy. In NETs, this therapy is carried out in several cycles (most often four to six), with several weeks or months in between.

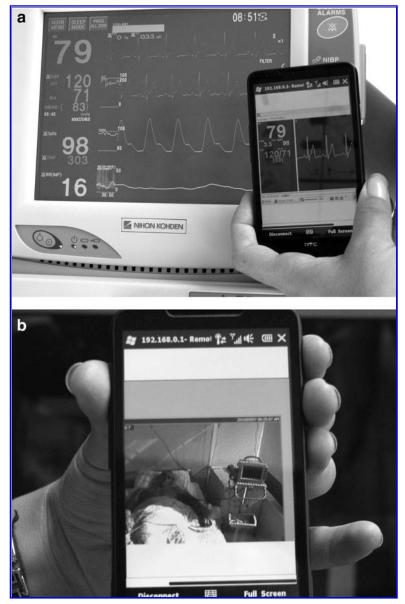
In Serbia, only 100–150 therapeutic doses for peptide receptor radiopharmaceutical therapy are applied yearly because of various limitations, even though the demand is higher. Together with DTC and NET patients, this amounts to 600–700 radionuclide therapeutic doses per year in Serbia. In our research, we stated that about one-fifth of our patients had changes of the vital functions detected by the telemonitoring system, so it can be estimated that around 150 patients a year require their vital functions to be monitored in this way. Needless to say, at a global level this number is far greater.

In Serbia, high-dose radionuclide therapy for treatment of DTCs and NETs could be administered only by nuclear medicine specialists trained for work with open sources of ionizing radiation. In other countries, administration of radionuclide therapy is allowed also by radiation oncologists (European Union) and by radiation oncologists and radiologists (the United States). In spite of large numbers of patients who need radionuclide therapy,

just a few health facilities in Serbia are appropriately equipped and staffed for this type of treatment. Administration of radionuclide therapy is a complex medical and organizational procedure, including all aspects of staff education and training, specific accommodation requirements, equipment requirements, costs, etc. Too often the continual presence of qualified physicians at the patients' premises could not be provided, taking into account the small number of nuclear medicine specialists. Therefore, good organization of work is extremely important for increasing the capacity of nuclear medicine departments for administration of radionuclide therapy. In some hospitals, including ours, implementation of a telemonitoring system could partially compensate for a lack of trained nuclear medicine specialists. With this system, the responsible physician is continuously present in close vicinity of the physical isolation area during and for the first day after administration of a radionuclide and afterwards is off duty but on call. The responsible physician is monitoring the patient and his or her vital functions from his or her computer at home or from his or her mobile phone and is from time to time contacting the patient by phone, in order to get better insight in the patient's health state. During this period, in the vicinity of the physical isolation area there is a nurse on duty, who contacts the physician on call in case of adverse events and treats the patient according to the physician's instructions.

Using our telemonitoring system we insure that the signals from vital functions of the patient, as well as from video surveillance cameras in the physical isolation area, are at each moment accessible remotely by the physician responsible for the patient treated with a radionuclide. In this way, the physician is able to check the patient's heart rate, electrocardiogram, blood pressure, respiration rate, and oxygen saturation

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**Fig. 5. (a)** Signals from the Nihon Kohden BSM-2351 Bedside Patient Monitor on the HTC HD2 mobile phone (using VPN and RDC connections). **(b)** Live video from the surveillance camera on the HTC HD2 mobile phone (using VPN and RDC connections).

at any time, using his or her personal computer or mobile phone. In addition, with this system, we can record video surveillance of the physical isolation area as well as of the patients' vital signs and later (offline) review and analyze the data. Staff costs are reduced with this system, leading to significant savings for the health facility.

Although there are articles that dispute the benefits of patient telemonitoring in ICUs,<sup>37,38</sup> some other authors' experiences<sup>29,39–41</sup> mostly support our results obtained by means of the telemonitoring system. For example, Thomas et al.<sup>37</sup> carried out an observational study on six ICUs that included 2,034 patients and found that remote monitoring of patients in the ICU was not accompanied by an overall

increase in mortality rates or a decreased stay in the ICU. Similarly, based on his study carried out in 2010, Dressler<sup>38</sup> reported that the use of remote ICU monitoring is often a consequence of the lack of intensive care physicians, as well as that it often fails to improve the outcome, which is why it cannot make up for the lack of personnel.

However, Maiolo et al.<sup>29</sup> researched the feasibility of telemonitoring in patients with severe respiratory diseases. They compared the results of face-to-face monitoring, in which physicians visited their patients in the first stage, and the telemonitoring of their condition by means of arterial oxygen saturation and heart rate control, done over the phone, in the second. The authors recorded a decrease in hospital admission and acute illness exacerbations by approximately 50% and a 17% decrease in medical bills when telemonitoring was used instead of face-to-face follow-ups done by physicians.

Breslow et al.<sup>39</sup> researched whether commercial telemedical and information systems in ICUs can improve clinical and economic performance of these units. Their research included 2,140 patients from two ICUs, and they found that with telemonitoring there was a decrease in mortality and hospital stays, as well as in medical bills.

Lilly et al.<sup>40</sup> examined the outcomes associated with the implementation of ICU TM among 6,290 adult patients admitted to seven ICUs. They reported that TM was associated with lower rates of ICU-acquired complications, hospital mortality, stay duration, and the duration of mechanical ventilation.

Young et al.<sup>41</sup> did a meta-analysis of the data obtained from 13 studies that included 35 ICUs with the total of 41,374 patients. Their results point to the fact that mortality rate, as well as the length of the hospital stay, decreased in cases where ICUs have telemedical support, compared with those that do not.

Certainly, TM cannot replace a physician, but may increase his or her efficiency and ease his or her everyday job. The responsible physician still has to enter the physical isolation area and help the patient in case of a real emergency or other imminent medical need, but with the help of telemonitoring the moment of interaction with the patient could be determined and scheduled with more precision and objectivity.

However, the communication between the physician and the patient should also be one of the foci, as research by Onor  $14^{2}$ 

et al.<sup>42</sup> points to the fact that videoconference interviews are less realistic and significantly different from face-to-face contact. Liu et al.<sup>43</sup> emphasized that new training programs are needed for doctors to develop improved communication skills and the ability to express empathy in TM consultations.

#### Conclusion

From our experience gained over the past 3 years, this model of organization and supervision by a telemonitoring system of a patient receiving radionuclide therapy insures a high level of safety for the patient, with significant reduction of staff costs.

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## **Disclosure Statement**

No competing financial interests exist for any of the authors.

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