

An innovative telemedicine approach to substitution and drug control

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Zusammenfassung

Telemedizinische Verfahren finden auf einem breiten thematischen Feld allmählich auch Zugang in die Suchttherapie, sind dabei aber noch deutlich unterrepräsentiert. Manifeste Probleme treten dadurch vor allem in strukturalarmen Gebieten mit einer entsprechend geringen Dichte von Suchtmedizinern und flächendeckend in Situationen auf, in denen der direkte Arzt-Patient-Kontakt ein schwerwiegendes gesundheitliches Risiko wie in der aktuellen COVID-19 Pandemie darstellt.

Für die Kontrolle von Drogenmissbrauch oder die Substitutionstreuung werden in den meisten Fällen Urinproben unter unmittelbarer Sichtkontrolle verwendet, was zu dem erwähnten Infektionsrisiko und häufig zu psychogenen Störungen führt. Alternativ wurden bisher Polyethylenglycol-Marker (PEGM) eingesetzt, bei denen der Patient den Marker unter Sichtkontrolle einnimmt und die Miktion ohne direkte Kontrolle erfolgt. Der individuelle PEGM findet sich bei der Analyse als Ausschluss der Nutzung von Fremdurin.

Kürzlich wurde für die PEGM-Einnahme ein Verfahren entwickelt, das zusätzlich auf eine direkte Kontrolle verzichtet und damit vom Patienten überall durchgeführt werden kann. Dies geschieht mit Hilfe seines mobilen Telefons und einer spezifischen Applikation. Die standardisierte Einnahme wird dabei als Video aufgezeichnet, per Block-Chain-Technologie verschlüsselt und an den betreuenden Arzt geschickt, der die Ordnungsgemäßheit der Einnahme überprüft. Dieses Verfahren wurde bereits an einer kleinen Gruppe von Patient*innen geprüft und soll jetzt einem größeren Kreis von Ärzt*innen zugeführt werden.

Schlagnote: Telemedizin, Substitution, Drogenmissbrauch, Urinmarker

Abstract

Telemedical procedures are gradually gaining access to addiction therapy in a broad thematic field, but are still significantly underrepresented. As a result, problems arise particularly in structurally poor areas with a correspondingly low density of therapists and across the board in situations in which a direct doctor-patient contact represents a serious health risk, as in the current COVID-19 pandemic.

As a standard, urine samples under direct visual control are sampled to control drug abuse or compliance with substitution, which leads to the risk of infection as with COVID-19 and often to psychogenic disorders. As an alternative, polyethylene glycol markers (PEGM) can be used, in which the patient takes the marker under visual control and urination takes place without direct control. The individual PEGM has to be present in the urine sample as an exclusion of the use of false clean urine.

Recently, a procedure was developed for taking PEGM, which needs no direct control and can therefore be carried out by the patient anywhere and without a human-human contact. This is done using his mobile phone and a specific application. The standardized intake is recorded as a video, encrypted using block chain technology and sent to the doctor in charge who checks that the intake is correct. This procedure has already been tested on a small group of patients and is now ready to be given to a larger group of therapists.

Keywords: telemedicine, substitution, drug abuse, urine marker

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1 Current situation

Telemedicine procedures and applications have increased their influence in society and thus also in addiction treatment in the last few years.

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We now have a variety of addiction treatment approaches to choose from in this area, ranging from phone-based support (McKay et al. 2004) to mobile apps for digitally connecting patients, the personal environment, and treatment providers (Hochstatter et al. 2019), from automated, timely detection of threatening relapse (Kornfield et al. 2018) to virtual worlds (Molfenter et al. 2015) and web-based videoconferencing (Tarp et al. 2017). However, growth remains far

behind the rate of globally booming digitisation. A study by Molfenter et al. (2012) found a low share of telemedicine in the overall therapeutic action for addiction medicine. The authors concluded that the field of addiction treatment as a whole has a lot of work to do to prepare for a future environment with high expectations regarding the use of information technologies, in particular in the context of responsible interaction with patients in terms of integrated care adjusted to the situation at hand. The high topicality of the current substitution situation is highlighted by the recently published 10-cornerstone paper on solutions for the supply crisis. It highlights some existing gaps in supply, proposing a modular toolbox for regional approaches (ISOP 2020).

The current situation of the SARS-CoV-2 pandemic has shown just how fragile care can be when the majority of it is based on direct personal contact between patients and therapeutic staff. The JES Federal Board, in association with Deutsche Aidshilfe, directed an open letter to the Kassenärztliche Vereinigung (Association of Statutory Health Insurance Physicians), asking to raise awareness among physicians working in addiction treatment for the high number of drug addicts who are high-risk patients for COVID-19 due to pre-existing infections such as HIV and HCV (JES 2020). The conference of the chairpersons of quality assurance commissions of the Kassenärztliche Vereinigungen in Germany reminded substituting physicians that their practices could serve as “potential centres for spreading the new coronavirus among the staff and the patients, in particular in light of daily administration of the substitute at sight” (KBV 2020). Accordingly, administration for “stably substituted” patients was to be extended from 7 to 14 or even 28 days. For non-stable patients, the therapist had to decide whether to issue weekly prescriptions for 2 days. In the end, this was a matter of “pragmatically balancing the need to ensure care with the need to ensure protection from infection, under consideration of narcotics safety (KBV 2020).” Another option recommended was administration of a buprenorphine depot, in which case substitution could last for up to one month (DAZ 2019). As can be seen, the critical moment in the current SARS-CoV-2 situation is the frequency of physical interaction between people.

2 Drug and substitution control using urine samples

No matter what kind of administration of substitution treatment is chosen, successful medium- and long-term therapy always makes it necessary to monitor the patient’s compliance. Urine remains the most commonly used matrix in monitoring drug abuse and proper use of substitution medications (Vindenes et al. 2011) since many substances can be detected for several days, analytical laboratories and physicians are familiar with the results, and a plethora of data is available in literature (Jufer et al. 2006). However, relevant results require proper delivery of autologous urine. Visual inspection, which requires a distance of no more than 1.5 metres between client and inspector when applied seriously, often not only violates the psyche of both client and inspector (Jones et al. 2015), but also comes with a risk of transmitting infections. An alternative method has been in use for several years. It involves individualising the urine by prior ingestion of a defined mixture of short-chain polyethylene

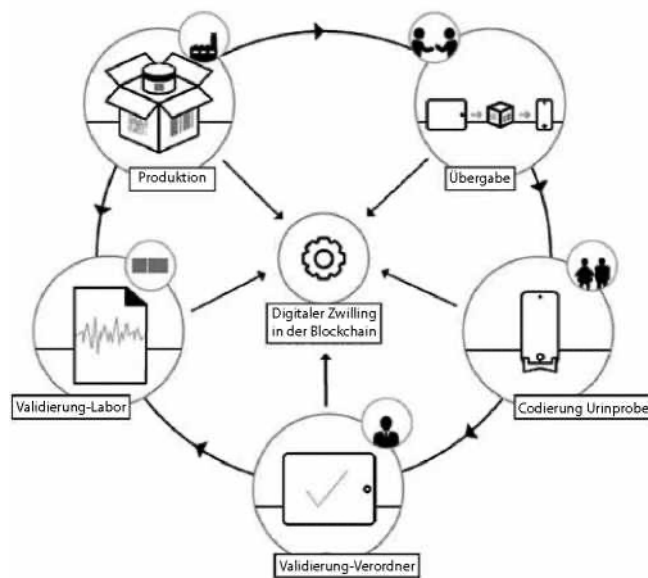
glycols that are not metabolised. Urination is then possible unsupervised after a waiting period of at least one hour. Kinetic analyses are available for this method (Baum et al. 2017); its acceptance among therapists and clients is high (Baum et al. 2018), and its susceptibility to interference by amount and composition of food or amount of fluid intake has been tested in a large collective (Einwächter et al. 2019). The latter study showed that markers could be detected in every case, in spite of a vast variation of interfering variables. The influence of interfering substances on drug detection was investigated by Huppertz et al. (2018). Both substances designed to produce a false-negative result and others meant to interfere with the analysis as such were taken into account for it. Strong bases and acids as well as oxidants interfere with analysis but are detected in the procedure, which permits marking the sample as having been tampered with. This method avoids the psychological issue of direct visual contact while preserving high analytical certainty. However, physical proximity between client and examiner remains necessary during capsule intake.

3 The RUMA digital system, the telemedical next step of urine marker technology

A system combining the advantages of marker technology and telemedicine in urine monitoring has been developed under the scientific leadership of Prof. Dr. Dr. Ruprecht Keller for several months, independently of the current pandemic. It generally involves telemetric recording of PEG capsule intake using mobile phones with integrated cameras. The patient only needs to have direct contact with the therapist during initialisation. The physician can mail the capsules for subsequent urine tests to their patient, just as the patient can mail their urine samples to the laboratory. This was originally planned to become an application for patients in rural areas, where considerable distances may need to be crossed to the examination facilities. In the SARS-CoV-2 crisis, however, it has provided an opportunity to capture, and thus support, treatment compliance among all eligible patients without exposing them to a risk of infection. The system operates at the highest current standard of data security (creation of a digital twin using blockchain technology) and a high level of procedural security (> Figure 1).

3.1 Warranting procedural security

> **Figure 1** shows how the process flows of telemetric urine marker monitoring interlock. All data communication is encrypted in a blockchain. The individual processes are elaborated below.



Produktion	Production
Übergabe	Handover
Digitaler Zwilling in der Blockchain	Digital twin in the blockchain
Validierung Labor	Laboratory validation
Codierung Urinprobe	Urine sample coding
Validierung Verordner	Prescriber validation

Figure 1: Flowchart of urine control by marker and telemetric detection of marker intake from production to process validation

3.1.1 Production

Ruma marker capsules are produced individually coded with interlocking security features on the outer and inner packaging and distributed to affiliated practices or facilities. The codes are provided to the laboratories at the same time. The code on the outer packaging (A code) has 32 characters, which cannot be decoded by unauthorised persons. It contains no information on the marker used. The code on the inner packaging (B code) has 8 characters. Only the blockchain records which PEG marker constellation has been assigned to the patient. The A and B codes are inseparable. The B code confirms that the correct patient has taken the correct marker from the correct packaging. Early removal or swapping of the marker would destroy the barcodes, rendering proper video recording of marker removal impossible (> **Section 3.1.3 Urine sample coding**). This means that the PEG marker can only be taken by the respective patient, preventing the delivery of foreign urine.

3.1.2 Marker handover

The practice/facility links the patient's app to the practice app once and provides training on handling and timing of the system. This contact includes recording of a current facial photo of the patient by the practice to permit assignment of subsequent video recordings of marker intake to the respective person. This contact ends with handout of the urine markers to be used.

3.1.3 Urine sample coding

Video-recorded marker intake takes place in the following steps:

Step 1

The patient places their smartphone in the stand provided to ensure that the camera can view the table, the utensils on it, and the patient's upper body. The procedure commences by starting the app and the confirmation of "Start intake". The smartphone camera is activated, and the patient can see themselves on the display.

Step 2

The patient opens the marker box (outer packaging) and places the inner packaging of the marker (marker container), the glass of water, and the chewy sweet provided in the camera's field of view.

Step 3

The patient scans the code on the outer packaging (A-QR code). A green checkmark appears in the display to confirm that the physician assigned precisely this marker box to the patient and that they are authorised to take that marker.

Step 4

The patient now scans the B code on the inner packaging (B-QR code). This is where recording of the max. 120 seconds long intake video begins. The patient takes the marker. During this time window, the patient needs to a) swallow the marker, b) chew the chewy sweet, and c) present their tongue with their mouth open. If the patient attempts to store the capsule in an oral pocket for later removal, the rapidly dissolving capsule shell will release a colouring agent (blueberry extract) that will dye the entire oral cavity blue.

Step 5

The video is encrypted and transmitted to the supervising physician's office. The patient will collect a sample of their next urine independently of location and send it in or hand it over to the laboratory.

Prescriber validation

The prescriber will review the marker ingestion video for correct ingestion or possible tampering asynchronously. Any possible indications of manipulations are documented. This also enables early support for the patient in cases of misconduct. The patient will be informed about successful completion of the process or about any issues with the transfer.

Laboratory validation

The laboratory will complete the accredited urine analysis. This includes verification of the marker code as well as specific tests for tampering.

3.2 Initial test runs with the RUMA digital system completed

Initial field trials of the feasibility of the RUMA system were performed in two German centres and in cooperation with A-Clinic Ltd in Finland. Finland was chosen to supplement the German sites because telemedicine shows a much higher penetration of the healthcare system there and the participating medical staff have

more comparative experience to draw on. A total of 19 patients (10 women and 9 men, age 42.6 ± 4.1 years; mean $\pm$ standard deviation) were chosen for the initial feasibility test. The patients were instructed in the procedure by the supervising clinic and subsequently performed the entire procedure at home on their own. They completed a questionnaire with six questions that was anonymised for the authors. The first four questions were scales from 0 to 10. Question 1 related to the introduction and explanation of the RUMA digital system by the medical staff (0 = entirely incomprehensible, 10 = perfectly comprehensible). The median score was 10. Handling the application received a median score of 9 (0 = extremely complicated, 10 = perfectly easy), handling the marker intake from starting the video recording to sending the video had a median score of 8 (0 = extremely complicated, 10 = perfectly easy), and marker urine control with video control received an overall median score of 9 (0 = extremely poor, 10 = extremely good). Questions 5 and 6 referred to issues encountered and suggestions for improvement; they allowed free text input. The most frequently cited issue was with scanning of the codes. This explains the comparatively low rating of question three. The procedure has since been modified to ensure that the mobile phone's camera can reliably recognise the code. Some patients requested a different consistency of the chewy sweet as improvement.

4 Outlook

The Ruma digital system will not be suitable for all patients. Some people, for example, may strictly refuse telemedical monitoring. However, those who do use the system can benefit from it in a variety of ways. It eliminates the need for visual inspections that violate privacy, strengthening personal responsibility and dispensing with the time previously lost by potentially long distances to be travelled to and from the medical care centres. Medical staff also benefit from elimination of visual inspection and can focus more on other tasks such as psychotherapeutic care. In the end, the entire control system is rendered more efficient this way: Intervals between notification of a subsequent urine test and urine collection can remain short and unpredictable. They only require sending a push message to the client's mobile phone.

Following successful initialisation of the system, it is now to be made available to a larger group of physicians. The system is going to be evaluated by physicians and patients and further optimised with the results from a clinical observational study.

Conflicts of interest

Klaus Baum is a scientific advisor of RUMA GmbH.

Kaarlo Simojoki received fees for scientific lectures and travel expenses from RUMA GmbH.

All other authors declare that they have no conflicts of interest.

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