Development of an Intelligent Tele-Diabetology System

PhD thesis

by

Mihály Dió

Semmelweis University
Doctoral School of Pathological Sciences

Supervisor:	Dr Tibor Deutsch, CSc, professor
Official readers:	Dr Sándor Nagy, reader, PhD Dr Márta Veressné Bálint, reader, PhD
Chairman of the Committee:	Dr Iván Forgács, CSc, professor emeritus,
Members of the Committee:	Dr Ildikó Nagy Baji, reader, PhD Dr Erika Erdősi, reader, PhD

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1. INTRODUCTION

According to a 2015 review by the International Diabetes Federation, 415 million adults live with diabetes in the world, and the number of children having diabetes have exceeded half a million. Nearly 6 percent of the Hungarian population is affected by diabetes, and the costs of care for patients constitute a considerable part of health expenditures all over the world. The overwhelming part of expenditures is due to complications (limb amputation, visual impairment, vascular diseases) and acute diseases (myocardial infarction, stroke etc.). Various multi-centre studies have clearly demonstrated that adequate care may considerably delay, and in many cases even eliminate, these serious complications of the disease. To this end, patients' blood glucose level must be maintained within pre-specified limits.

In patients having type 1 diabetes (T1D), the pancreas does not produce insulin at all. For this reason, these patients need insulin administration. Insulin products of different action times are available for such treatment. Insulin dosage titration is based on regular self monitoring of blood glucose levels (SMBG). This requires various blood glucose meters as indispensable instruments. Three-quarters of the currently used glucometers can upload measured data to a computer for storage and analysis. In addition to the blood glucose values, in an ideal case, the insulin doses and descriptions of hypoglycemic episodes along with supplementary comments are also entered in the patents' electronic logbook.

In general, patients consult their physicians once in 2-3 months. During such visits, the care providers analyse the recorded data in order to reveal control problems (if any), try to assess their causes, and if required, propose a modification in the current management regimen. Between visits patients frequently apply 'corrective doses', e.g. in cases when their current blood-sugar level is extremely high or when they plan to consume significantly more carbohydrates than usual. In other cases the insulin dose needs to be adjusted because of special blood glucose patterns persisting for several days (blood-sugar pattern management).

Despite the widespread application of modern insulin preparations and glucometers, a high number of diabetic patients are inadequately controlled. This may have various reasons. During the short time available for a visit, physicians often find it difficult to interpret large number of home monitoring data and to select the most appropriate therapy. Large number of patients are also clearly accountable for failures, as many of them do not follow the physician's recommendations. Unfortunately, most control problems are only revealed during visits. In such cases, even the most accurately maintained logbook only documents the problems that should have been prevented.

The various tele-medicine systems offer an excellent solution for the above-mentioned information management problems. Nowadays, there is a high number of web applications that enable patient to send the measured blood glucose values to a computer, where a program ensures data receipt and the up-to-date maintenance of the management log. In addition, these modern systems facilitate the analysis of SMBG data and the solution of any treatment-related problems.

Among others, 77 Elektronika Kft offers extensive services for Dcont users. With an infrared port or through an USB cable and a computer, the system is able to upload the BG values into an online database, and compiles statistical summaries, graphic diagrams and descriptive statistics upon request. In m-health systems, applications installed on mobile instruments (e.g. smart phones) analyze data and give advice when required.

Some tele-diabetology systems described in the literature provide services which go beyond data visualization and statistical summaries. Certain systems offer data interpretation services in order to extract relevant blood glucose patterns inherent in SMBG data. These programs typically apply time series, pattern recognition and temporal abstraction as methods to reveal problems in patient data.

Naturally, the ultimate goal of telemedicine systems is to assist problem solving as part of diabetes management process. Therefore, the various decision-support services play an outstanding role in such systems. Most of these services are related to the modification of insulin dosage regimens. Typically, insulin dosage adjustment relies on either "if... then..." type production rules or mathematical models of carbohydrate metabolism adjusted for the particular diabetic patient.

One of the essential limitations of the widely used summary statistics is that they completely ignore the interrelationship between the blood glucose values measured at various times. It is obvious, for example, that the subsequent blood glucose measurements are not independent of one another. Completely different conclusions are drawn from a 9.5 mmol/l blood glucose value measured before lunch if the morning blood glucose value was 4.6 mmol/l or 17.3 mmol/l.

Another essential problem is the casual nature of statistical analyses. Physicians and patients alike are free to analyse the recorded data in many different ways, however, the conclusions drawn without a standard method will necessarily be accidental. Intelligent data analysis methods are required for obtaining relevant and sound information hidden behind recorded data.

In the course of my work, I made efforts at closing this methodological gap. I paid special attention to ensuring that the elaborated procedures can also be applied to the Dcont glucometer, widely used in Hungary. I was provided an excellent background to this by the cooperation agreement signed with 77 Elektronika Kft.

2. OBJECTIVES

I intended to develop various data analysis and decision-support methods that facilitate the complex analysis of SMBG data, the systematic identification of control problems, and the determination of situation-specific insulin dosage in T1D patients. The specific research goals included the development of the following methods:

- a methodology for the comprehensive analysis of SMBG data
- a method for testing the consistency of recorded data
- a method for identifying and diagnosing compliance and glycaemic control problems inherent in SMBG data
- a set of intelligent data analysis procedures for obtaining informative patterns inherent in SMBG data
- a set of methods for the determination of corrective insulin doses in pre-specified situations during the diabetes management process
- a method for the determination of corrective insulin doses in any situation during the control process based on the current blood glucose value and the last administered insulin dose, and
- a method for the determination of insulin dosage adjustment as part of blood glucose pattern management.

3. METHODS

The elaborated methods were tested using SMBG data sets recorded by five T1D patients for 2-3 months. The time series come from patients treated at the Diabetes and Endocrinology Service of the St Thomas Hospital in London. These data series included pre- and post-prandial blood glucose values related to main meals, blood glucose values measured at night along with insulin doses. As patients recorded deviations from the usual diet and exercise only occasionally, life style information was not considered in data analysis.

Data analysis methods

I used various descriptive statistics to summarize the recorded blood glucose readings. For knowledge-based data interpretation, various data-abstraction, pattern-recognition and temporal reasoning procedures were used. The basic idea was that the most relevant clinical information inherent in SMBG data is reflected by various temporal blood glucose patterns. I determined blood glucose patterns by abstracting the recorded values. Various state and change abstractions were dominantly used. One of the important cases of change abstractions is the trend in BG data. For instance, when the daily mean blood glucose values exhibit a persistent increase in the past two months.

By combining elementary abstractions, I defined numerous complex abstractions (patterns). For example, the rebound effect was specified as a pattern of a low blood glucose level followed by several high blood glucose readings. An important example of complex abstractions is the daily blood glucose balance profile. In the case of a profile marked by (p, p, z, n), the blood glucose level rises between breakfast and lunch as well as between lunch and supper (the glucose balance is positive (p) > 3 mmol/l), the balance is nearly zero (z) between supper and bedtime, and during the night the blood glucose level falls considerably (the drop is > 3 mmol/l). Naturally, the threshold value can be freely set (e.g. at 2 mmol/l instead of 3 mmol/l).

Rules-based decisions

In order to select treatment decisions, various knowledge representation and manipulation procedures were used. Insulin dosage were determined on the basis of rule-based (logical) and model-based reasoning.

In the case of simple decision-making rules, one specific therapy is assigned to a specific blood glucose pattern. For example, if the daily mean blood glucose value is high, the basal insulin should be increased. As a general rule, the insulin component with the maximum effect in the given period should be modified.

I specified knowledge about corrective insulin dosage in the form of rules. When the patient eats more than usual carbohydrate, and the amount of the additional carbohydrate is known, the corrective insulin dosage is calculated using the carb:insulin ratio. For example, if the carb:insulin ratio is 15:1 and the additional carbohydrate is 60 g, then 4 U of short-acting insulin is required to offset the expected rise in blood glucose level.

I used ‘Rule 1500’ to determine the insulin sensitivity (IS) of individual patients:

IS = 1500/ (18 * ID) mmol/(lit U)

where ID is daily insulin dose and IS stands for decrease in the blood glucose level (mmol/l) after the administration of 1 unit of short-acting insulin. As the insulin sensitivity is different for every person, the insulin dosage advice can be customized if this formula is used.

Similar rules were used to specify the additional carbohydrate intake which is needed to prevent imminent hypoglycemia in cases when the patient is planning physical activity. Naturally, the extent of adjustment depends on the intensity and duration of the physical activity. The information required for pattern management was specified in decision-tables in the PROLOGA system.

Pattern management enables us to solve control problems persisting for more than one day (e.g. if evening blood glucose values are very high on three successive days). In such cases there is no need to wait until the next visit to modify the relevant insulin dose. Maximum 10% adjustment in the insulin dosage is allowed on one occasion.

Pharmacokinetic model of insulin

The aforementioned rules can only be used in pre-specified situations. In the course of self-management, there may be numerous situations in which general rules don't offer any guidance. In such cases the insulin dosage was calculated with the help of a pharmacokinetic model of insulin.

Following the administration of a sc injection, dimeric insulin is absorbed into the systemic circulation. Its further fate depends on insulin distribution and elimination dynamics. The pharmacokinetic model of insulin included compartments such as the heart, brain, liver, kidney, muscle and fatty tissues. I described the distribution of insulin in every organ by the 'two-compartment model', i.e. taking the distribution of insulin between blood and the interstitial fluid into consideration. In the liver and in the kidney, insulin is metabolized and excreted from the body. I adopted blood flow rates and the characteristic parameters of insulin transport and elimination processes within the individual organs from a validated model.

I described the absorption of different insulin preparations using a generic model. This model is suitable for grasping the essential physical and chemical processes at the site of administration for all available insulin products, including fast-acting and very long acting insulin analogues. I used the MATLAB™ program for simulation purposes. For numeric integration the Euler method (step size = 0,01 minute) was used.

During the calculation of insulin doses, I presumed that the effect of insulin in a given time interval is proportional to the area under the plasma insulin vs time curve.

4. RESULTS

One part of the results achieved during my work is related to the complex analysis of SMBG data. The other part includes the procedures used for the calculation of insulin dosage.

Complex analysis of blood glucose data

The data recorded by patients serve as the raw material for intelligent data analysis. The blood glucose data within a given time interval are displayed as a tabular daily breakdown. The cells of the table show the specific meter readings at a given time. Different colours were used to highlight data that belong to different blood glucose categories (e.g. low, normal, etc.).

However, care must be taken if the blood glucose data are not in agreement with our expectations and/or with other data obtained during the care process (consistency checking). As the first step of the elaborated algorithm, I checked if the characteristic features of SMBG data are in agreement with the adjustments made in the insulin regimen (or life-style) at the preceding visit. If the patient's daily insulin dose has been increased since the previous visit, it would be astonishing to see blood glucose values continue to rise.

For the consistency checking I used a special histogram that clearly shows the impacts of insulin dosage modification on the distribution of blood glucose values obtained at various times of the day. The analysis of home monitoring blood glucose data can only be carried on if these data provide a consistent history.

Home monitoring data were analysed in the following three major steps:

- checking the appropriateness of monitoring
- analysis of blood glucose readings from different perspectives
- identification and ranking of problems that were detected

Quality of monitoring

The quality of monitoring was assessed using the number and temporal distribution of blood glucose measurements. Monitoring quality is obtained from the (1) total number of blood glucose tests, (2) the number of tests at the individual times (at night, before and after

breakfast etc.), (3) the number of test pairs in the individual times of the day (before breakfast / after breakfast, before lunch / before lunch etc.) and (4) the number of daily blood glucose profiles (the 5-point profile without post-prandial tests, the 8-pont daily profile including post-prandial blood glucose tests).

These descriptive statistics enable us to establish how closely the patient has followed the physician's prescriptions.

Analysis of blood glucose readings

The blood glucose data recorded by patients are analysed according to the following criteria:

Criterion 1: General quality of blood glucose values in comparison to the objectives

- mean and median of blood glucose values
- percentage of the blood glucose levels that are lower than the limit of the specified target ranges, percentage falling within the range, and percentage of values exceeding the upper limit of the target range
- average pre- and post-prandial blood glucose values in each landmark time of the day, per meal and aggregated.

Criterion 2: Variability of blood glucose values

- standard deviation and variation coefficient of blood glucose values, their lowest and highest values, range
- percentiles and the interquartile range
- frequency of blood glucose valued falling in various ranges during different times of the day

Criterion 3: Episodes of hypo- and hyperglycemia

- total number of hypoglycemias/hyperglycemias
- number of hypoglycemias/hyperglycemias in the individual times of the day (in the morning, in the afternoon, in the evening, at night).
- severity of hypoglycemias/hyperglycemias

Criterion 4: Data patterns

In the course of intelligent data analysis, the time, frequency and nature of patterns in SMBG data were studied. These patterns are similar to the categories physicians use in an effort to grasp characteristic features of data between two successive visits.

For example, interesting patterns include the hypoglycemic state (the number of hypoglycemic episodes + the number of measured hypoglycemic blood glucose values in a week exceed a critical value (e.g. 3)), the positive/negative glucose balance (there is a difference (increase or decrease) exceeding 3 mmol/l between two successive pre-prandial values), the dawn phenomenon (the blood glucose value taken before breakfast exceeds a critical limit (e.g. 12 mmol/l) and the blood glucose value measured at bedtime falls within the normal range and there was no hypo- or tested low glucose value during the night) or the unbalanced daily blood glucose profile (difference between the highest and the lowest daily pre-prandial blood glucose values exceeds 3.5 mmol/l). One of the most important goals of SMBG data analysis is the compilation of the daily blood glucose profile.

If the user wants to know the evolution in blood glucose levels in the past three months, the trend line or the histogram of daily averages are to be displayed. If the focus is on daily fluctuations, the characteristics of maximums and minimums need to be analysed. Various patterns and indicators may be assigned to various perspectives in which different abstractions may be used. If, for example, blood glucose levels have increased in the past 3 months, but the daily profiles typically remained balanced, the clinician will be given a brief summary of what has happened to the patient in the period since the last visit.

Problem identification

The ultimate goal of analysing SMBG data is to reveal various control and compliance problems. Problems may be established from the patterns identified during data analysis. Problems may arise in relation to the metabolism, life-style, compliance, and self-management and their combination.

Problems include, for example (1) nocturnal hypoglycemia (one is sufficient), (2) frequent hypoglycemia (in any time of the day, except night, the number of hypoglycemic episodes + the number of measured hypoglycemic blood glucose values exceed a critical limit (e.g. 3) within a week, (3) high blood glucose variability (there are more than a given number (e.g. 2) of hypoglycemic episodes in a week, and more than a specified percentage (e.g. 60%) of the blood glucose values is hypoglycemic or the standard deviation of blood glucose values

exceeds 0.33 x blood glucose mean, or (4) insufficient monitoring (the number of tests performed is much less than the recommended monitoring frequency).

Naturally, in the last phase of the data interpretation process, the cause of the problems must be found. To this end, I used special visualization methods that help identify a correlation between the revealed patterns, the patient's life-style, compliance, and treatment. In the course of pattern management, root causes are easier to identify if BG data are displayed with focus on the proximity of the period reviewed.

Diagnosing control problems is frequently difficult. In certain cases several explanations may come into focus, which may require conflicting therapy modifications. For example, if fasting hyperglycemia is caused by the dawn phenomenon, bedtime insulin dose must be increased. However, one should not disregard the option that morning hyperglycemia may be caused by a Somogyi effect triggered by the previous day's hyperglycemia.

Modification of insulin dosages

In the course of my work problems were assumed to be corrected by adjusting the relevant insulin dosage. The general strategy serving this end is to first make efforts at the elimination of blood glucose fluctuations, and when the daily rhythm is sufficiently smooth, the mean level is shifted towards the target range. Each dosage adjustment method takes the variability of individual insulin sensitivity into consideration.

The insulin bolus calculator is suitable for the calculation of modified insulin doses if (a) the patient's current blood glucose value considerably differs from the target value given for the specific time; (b) the patient is about to consume considerably more carbohydrate than usual; and/or (c) during the given day the patient plans to do considerably more physical activities than usual. I described the conditions and the related interventions with the help of decision-tables.

I elaborated a special insulin algebra that can be used at any situation. As a condition to application, the patient should test the current blood glucose value at the specified time and should accurately record the type and dose of the last administered insulin. This is required because if insulin dosage is calculated exclusively on the basis of the current blood glucose level, we may easily come to a false conclusion. In such cases the method I have developed takes the expected blood glucose reducing effect of the previously injected but not yet absorbed insulin into account. This effect is determined with the help of the area below the curve in the appropriate time interval.

CONCLUSIONS

SMBG is only successful if the data obtained are evaluated in time and fed back to the care process. This is true both during visits and in periods between physician-patient encounters. However, each actor in the diabetes management process need help both in the fast and reliable analysis of the large quantity of SMBG data and in the periodic or long-term modification of the care plan based on such analysis.

For this reason it is imperative to integrate the developed data analysis and decision-support procedures in the data management and decision-support modules of an intelligent tele-diabetology systems. The elaborated methods are easy to use in the web-based services relying on Dcont glucose meters, widely used in Hungary, if the manufacturer wishes to provide patients with more than mere data storage, statistical analyses and data visualization.

In such a system the services provided to patients facilitate the SMBG process and the required therapy modification. When the patient tests blood glucose, the content of the electronic care database is automatically updated, and the system checks if the data indicate any problem that must be addressed. The system sends a message to warn the patient that e.g. no blood glucose data have been sent for three weeks and insulin dosages are never modified despite the fact that based on his or her life-style, this is required. The system automatically reveals any control problem encountered. The system calls the patient's attention to the identified problems in the form of a message, or in more serious cases, by an alert message. Such a notice may include criticism (e.g. the morning insulin dose should not have been increased in this extent). In certain cases the system also makes suggestions (e.g. calculates the number of units to increase the short-acting insulin dose injected before a meal due to the additional carbohydrate consumed during lunch).

It is especially important for the patient to continuously see that the conducted blood glucose tests have a continuous impact on care rather than simply waiting in the log book for the physician to give them a glance during visits. It is also highly important to have custom-tailored therapy and monitoring proposals, as patients' long-term cooperation cannot be ensured by one-size-fits-all recommendations.

In the tele-diabetology system physicians have access to the obtained blood glucose, life-style and treatment data, before visits they can seek help for the interpretation of SMBG data and can see long-term trends and the relevant clinical patterns inherent in blood glucose data. With this system it is easier to obtain and analyze data, and select customized therapy. It is also highly important for them to be able to constantly monitor events in the patient's life and to intervene in processes whenever required.

The application of tele-diabetology systems is expected to improve the quality of care, however, the benefits and any disadvantages must be evaluated by carefully planned clinical studies. It is insufficient to document short-term improvement observed in the HbA1c value, service quality, effectiveness, cost-efficiency and long-term outcomes (e.g. complications) must also be evaluated.

The extensive use of tele-diabetology systems requires fundamental changes in financing. In the new model, achievements (e.g. decrease in Hba1c values) rather than service volumes (number of visits, costs of check-ups) need to be financed.

New achievements

The following list includes the results achieved during the research:

- I developed a general method for the comprehensive analysis of SMBG data. The new method covers the successive steps of data analysis, including the procedures required for displaying and interpreting information.
- I developed a new visual method for testing the consistence of blood glucose data and for the analysis of the effects of the applied insulin treatments.
- I defined the compliance and BG control problems encountered during care for T1 DM patients and the blood glucose patterns suggesting any of these problems.
- I elaborated new intelligent data analysis procedures for extracting and graphically displaying informative patterns hidden behind SMBG data.
- With the help of decision-tables, I defined rules for corrective/compensatory insulin dosages in cases when the patient's current blood glucose value and/or life-style considerably differs from the target/usual pattern. During the calculation of doses, I took patients' personal insulin sensitivity into account.
- With the help of decision-tables, I defined the rules of insulin dosage modifications required during blood glucose pattern management on the basis of blood glucose patterns observed on three subsequent days.
- I developed a new insulin algebra to determine a situation-specific insulin dosage with due consideration to the expected blood glucose reducing effect of the last insulin dose not yet absorbed. This procedure presumes that in a given time period the blood glucose reducing effect of insulin is proportionate to the area under the plasma level vs time profile, and inversely proportional to the patient's insulin sensitivity.
- I implemented a pharmacokinetic model of insulin absorption, distribution and elimination that reflect underlying physiology. Using the model the plasma insulin levels were computed over time following the sc injection of fast-, short, intermediate,

long- and very long-acting insulin preparations in a range of 1-60 units dosage. These insulin-time profiles were used for the calculation of insulin dosage.

AUTHOR'S PUBLICATIONS

Publications related to the thesis:

Dió Mihály, Deutsch Tibor, Mészáros Judit: In silico diabetológia, Orvosi Hetilap 157:(6) pp. 219-223. (2016)

Dió Mihály, Deutsch Tibor, Biczók T, Mészáros Judit: Vércukor önellenőrzési adatokra épülő intelligens infokommunikációs szolgáltatások a diabetes gondozásban, Informatika és menedzsment at Egészségügyben 15:(1) pp. 42-45. (2016)

Dió Mihály, Deutsch Tibor, Biczók T, Mészáros Judit: Vércukor-önellenőrzési adatok intelligens értelmezése, Orvosi Hetilap 156:(29) pp. 1165-1173. (2015)

Dió Mihály: A tele-diabetológia jelentősége és lehetőségei, Klinikai és Kórházi mérnökök országos konferenciája, Budapest, szeptember 27. (2014)

Dió Mihály, Deutsch Tibor, Mészáros Judit: An educational model of glucose homeostasis in diabetes mellitus, New Medicine 18:(1) pp. 29-32. (2014)

Dió Mihály: Intelligens tele-diabetológiai rendszer koncepcionális terve, In: Kósa István, Vassányi István (szerk.), Az e-Health kihívásai. A XXVI. Neumann Kollokvium kiadványa. 210 p. , Konferencia helye, ideje: Veszprém, Magyarország, 2013.11.22-2013.11.23. Veszprém: Pannon Egyetem, 2013. pp. 95-98. (ISBN:978-615-5044-90-8)

Dió Mihály: A házi ápolás (home care) eszközei, In: Dió Mihály, Szekrényesi Csaba, Zakár István, Zombory Péter, A biofizika és orvostechnika alapjai. 538 p. Budapest: Semmelweis Egyetem Egészségtudományi Kar, 2013. pp. 523-536. (ISBN:978 963 9129 93 1)

Dió Mihály, Deutsch Tibor, Meszaros Judit: Conceptual design of an intelligent tele-diabetology system, New Medicine, vol. XVII, 1/2013, p 28-30.

Publications independent of the thesis:

Lipienné Krémer Ibolya, Rados Melinda, Pálvölgyi Miklós, Dió Mihály, Mészáros Judit, Soósné Kiss Zsuzsanna: A highly demanding profession: midwifery. Do the midwives who provide sensitive support for birthing women feel satisfied and appreciated?, NEW MEDICINE 20:(1) pp. 19-26. (2016)

Antal Szabina, Lipienné Krémer Ibolya, Dió Mihály, Balogh Zoltán, Health education needs in the circle of roma population, In: Balogh Zoltán (főszerk), Papp Katalin, Hirdi Henriett (szerk.): 4th European Transcultural Nursing Association International Conference 2015: Reclaiming compassion at the heart of Nursing. 119 p. , Konferencia helye, ideje: Budapest, Magyarország, 2015.06.29-2015.06.30. (Magyar Egészségügyi Szakdolgozói Kamara (MESZK)), Budapest: Magyar Egészségügyi Szakdolgozói Kamara, 2015. pp. 107-108. (ISBN:978-963-89435-8-3)

Járfás Vivien, Lipienné Krémer Ibolya, Hoyer Mária, Dió Mihály: A szülés körüli történések hatása az anyai hangulatváltozásokra, XXIII. Országos Szülésznői Konferencia, Budapest, 2015. 05. 14-16., poszter (2015)

Lipienné Krémer Ibolya, Vincze Felícia, Dió Mihály, Mészáros Judit: Egészségmagatartási vizsgálat a szülésznők körében dohányzás, alkohol- és kávéfogyasztás tekintetében, INFORMATIKA ÉS MENEDZSMENT AZ EGÉSZSÉGÜGYBEN 14:(10) pp. 34-38. (2015)

Lipienné Krémer Ibolya, Dió Mihály, Mészáros Judit: Vajon a szülésznők körében is létezik a kiégés jelensége?, XXIII. Országos Szülésznői Konferencia, Budapest, 2015. 05. 14-16., poszter (2015)

Rados Melinda, Lipienné Krémer Ibolya, Dió Mihály, Kovács Eszter: Environmental and Social Privacy and Intimacy During Childbirth, In: Balogh Zoltán (szerk.), COHEHRE conference: Health and Social Care Perspectives for a Sustainable Future. Konferencia helye, ideje: Budapest, Magyarország, 2015.04.22-2015.04.24. Budapest: Semmelweis Egyetem, Egészségtudományi Kar, 2015. pp. 118-119. (ISBN:978-963-7152-93-1)

Ibolya Krémer Lipienné, Mihály Dió, Judit Mészáros: Burn-out research among midwives, NEW MEDICINE 28:(4) pp. 146-150. (2014)

Dió Mihály, Szekrényesi Csaba, Zakár István, Zombory Péter: A biofizika és orvostechnika alapjai, Budapest: Semmelweis Egyetem Egészségtudományi Kar, 2013. 538 p. (ISBN:978 963 9129 93 1)

Dió Mihály, Forgács Lajos: Egészségügyi-kórháztechnikai alapfogalmak.1.rész., ORVOS- ÉS KÓRHÁZTECHNIKA 45:(1) pp. 3-8. (2007)

Dió Mihály, Forgács Lajos: Egészségügyi-kórháztechnikai alapfogalmak.2.rész., ORVOS- ÉS KÓRHÁZTECHNIKA 45:(2) pp. 36-42. (2007)

Dió Mihály, Forgács Lajos: Egészségügyi-kórháztechnikai alapfogalmak.3.rész., ORVOS- ÉS KÓRHÁZTECHNIKA 45:(3) pp. 4-9. (2007)

Dió Mihály: Orvostechnikai eszközök kezelésének alapelve, In: Forgács Lajos (szerk.), Orvostechnikai eszközök: Gyakorlati útmutató I.kötet. Budapest: Semmelweis Egyetem Egészségtudományi Kar, 2007. pp. 79-99.

Dió Mihály: Légzésvizsgáló készülékek, In: Forgács Lajos (szerk.), Orvostechnikai eszközök: Gyakorlati útmutató I.kötet. Budapest: Semmelweis Egyetem Egészségtudományi Kar, 2007. pp. 190-206.

Dió Mihály: Terheléses vizsgálati munkahely készülékei, In: Forgács Lajos (szerk.), Orvostechnikai eszközök: Gyakorlati útmutató I.kötet. Budapest: Semmelweis Egyetem Egészségtudományi Kar, 2007. pp. 207-219.

Dió Mihály: Ultrahang diagnosztikai készülékek, In: Forgács Lajos (szerk.), Orvostechnikai eszközök: Gyakorlati útmutató I.kötet. Budapest: Semmelweis Egyetem Egészségtudományi Kar, 2007. pp. 271-299.

Dió Mihály: Milyen dokumentumokkal forgalmazható orvostechnikai eszköz?, ORVOS- ÉS KÓRHÁZTECHNIKA 42:(5) pp. 143-146. (2004)

Dió Mihály: Dokumentumok az orvostechnikai eszközök forgalmazásához, ORVOS- ÉS KÓRHÁZTECHNIKA 41:(1) pp. 18-20. (2003)

Dió Mihály: A 47/1999. (X.6.) EüM rendelet hatályát megelőző időszak orvos-technikai eszközökre vonatkozó okiratai és érvényességük, ORVOS- ÉS KÓRHÁZTECHNIKA 39:(2) pp. 36-54. (2001)

Dió Mihály, Haláchy Enikő: Kérdések és válaszok az új orvostechnikai eszközökről szóló rendeletről, ORVOS- ÉS KÓRHÁZTECHNIKA 38:(2) pp. 47-50. (2000)

Dió Mihály: Orvostechnikai eszközök alkalmazásának kritériumai, ORVOS- ÉS KÓRHÁZTECHNIKA 38:(3) pp. 71-76. (2000)

Dió Mihály: Szempontgyűjtemény műszerbeszerzésekhez, KÓRHÁZ ÉS ORVOSTECHNIKA 37:(5) pp. 180-189. (1999)

Dió Mihály: Ajánlott szempontok orvostechnikai készülékek vásárlásakor, KÓRHÁZ ÉS ORVOSTECHNIKA 36:(4) pp. 138-139. (1998)

Dió Mihály: Leggyakoribb kémiai áramforrások orvostechnikai készülékekben, KÓRHÁZ ÉS ORVOSTECHNIKA 35:(3) pp. 91-98. (1997)

Forgács Lajos, Dió Mihály: BUDAMED '96 Konferencia nemzetközi részvétellel, KÓRHÁZ ÉS ORVOSTECHNIKA 34:(6) pp. 195-198. (1996)

Forgács Lajos, Dárday Vilmos, Dió Mihály: Egy szakmai tanulmányút tapasztalatai, KÓRHÁZ ÉS ORVOSTECHNIKA 34:(1) pp. 28-34. (1996)

Forgács Lajos, Dió Mihály: A klinikai mérnök az egészségügyi intézményben, KÓRHÁZ ÉS ORVOSTECHNIKA 34:(3) pp. 61-68. (1996)

Forgács Lajos, Dárday Vilmos, Dió Mihály: Egy szakmai tanulmányút tapasztalatai, KÓRHÁZ ÉS ORVOSTECHNIKA 33:(6) pp. 287-292. (1995)