치과용 임플란트에 대한 ISO 14971 기반의 리스크관리

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Application of Risk Management for Dental Implants Based on ISO 14971

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Abstract : Risk management is the process that helps to identify hazards, analyze them, and then to create an action plan to avoid and mitigate these hazards. The main objective of risk management in product development and manufacturing is to provide safe and efficient products without spending too many resources. Medical device manufacturers also face enormous risks - regulatory, legal, and financial - based on their products and processes, and the concepts of risk management are particularly important because any single failure may result in serious damages to body or loss of life. In this regard, a set of guidelines for the application of risk management to medical devices has been issued by ISO and specified in the document ISO 14971 Medical devices - Application of risk management to medical devices. The main objective of this study is to investigate the application of risk management to dental implant development and manufacturing processes based on ISO 14971. A general risk management process is first introduced, and the application of ISO 14971 to dental implants is further investigated.
Key Words : risk management, ISO 14971, medical devices, dental implants, case study

1. Introduction

A dental implant has widely been recognized as one of the most innovative and efficient ways of restoring the masticating function of missing teeth. Prior to the advent of dental implants, a number of dental prostheses including bridges and dentures have been applied. Compared with the dental implants, these prostheses are readily inexpensive but causes a great deal of discomfort and inconvenience to patients. Furthermore, the jaw bone actually sinks away when teeth are lost, and just wearing dentures without bone supports may accelerate this process. Thus, the restoration of teeth roots supported by jaw bones may be far more beneficial in the long run. Dental implants appear similar to an actual tooth root and are placed within the drilled socket of jaw bone. Dental implants are usually made of titanium and osseointegrate with the jaw bones. The term 'Osseointegration' refers to the adhesion of the implant surface to surrounding bones. With the rapid aging and improved standard of living, dental implants have become a very popular choice for numerous patients although relatively expensive. It has been reported, in many clinical studies, that the success rate of installing dental implants ranges from 95% to 98%. Although the success of a dental implant is related to various factors such as operator skills, quality and quantity of the bone available, and the patients' oral hygiene, any single failure attributable to the product itself will be devastating. Thus, the responsibility of manufacturers is increasingly emphasized to ensure the product quality,

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safety, and efficacy.

Risk management is the process that helps to identify hazards, analyze them, and then to create an action plan to avoid and mitigate these hazards. The main objective of risk management in development and manufacturing is to provide safe and efficient products without spending too many resources, for example, for verifying and validating processes and equipments. Medical device manufacturers also face enormous risks - regulatory, legal, and financial - based on their products and processes, and the concepts of risk management are particularly important in relation to medical devices because of various stakeholder including medical practitioners, the organization providing health care services, governments, industry, patients and member of the public[1]. In this regard, a set of guidelines for the application of risk management to medical devices has been issued by ISO and specified in the document ISO 14971 Medical devices - Application of risk management to medical devices. The specifics of applying ISO 14971 may greatly differ with respect to the characteristics of medical devices under investigation in the sense that the types and scopes of risks are highly dependent on the product. The main objective of this study is to investigate the application of risk management in the development and manufacturing processes of dental implants and related surgical tools. Specifically, ISO 14971 is adapted to examine the applicability of relevant tools for identifying and controlling various risk factors. Most of existing studies on risk management of dental implants are concerned with the surgical treatments[2,3]. To the best of authors' knowledge, this study is the first to deal with the risk management of development and manufacturing processes for dental implants. A generic risk management process is briefly introduced, and the application of risk management to dental implants based on ISO 14971 is further investigated.

2. Generic Risk Management Process

According to ISO 14971, a risk is defined by the 'combination of the probability of occurrence of harm and the severity of that harm'. By definition, a hazard itself cannot result in harm until such time as a sequence of events or other circumstances lead to a hazardous situation. At this stage the risk can be assessed by estimating both severity and probability of occurrence of harm that could result. Thus a good starting point for risk management is to locate the sources of potential hazards and understand the mechanism leading hazards to hazardous situations. In general, risk management process consists of the following elements: risk analysis, risk evaluation, risk control, production and post-production information. First, risk analysis activities involve the identification of characteristics related to the safety of the medical device, identification of hazards, and estimation of the risk(s) for each hazardous situation. Some available techniques for the purpose of risk analysis include preliminary hazard analysis (PHA), fault tree analysis (FTA), failure mode and effect analysis (FMEA), failure mode, effect, and criticality analysis (FMECA), hazard and operability study (HAZOP), and hazard analysis and critical control point (HACCP). Detailed procedure and guides for the application of individual techniques can be found in the existing literature. For example, readers are referred to IEC 61025[4], IEC 60812[5], IEC 61882[6], Flick et al.[7] for detailed information on FTA, FMEA, HAZOP, and HACCP, respectively. Using these techniques, the probability of occurrence and severity of individual harms may be estimated quantitatively or qualitatively. Second, the purpose of risk evaluation is to decide whether risk reduction is required (i.e., whether a risk is acceptable or not) for each identified hazardous situation. Risk acceptability may be determined by using applicable standards, comparing levels of risk evident from medical device already in use, and/or evaluating clinical study data. Risk evaluation matrix is most commonly used to indicate acceptability criteria. When risk reduction is required, it is imperative to perform risk control activities such as risk control option analysis, implementation of risk control measure (s), residual risk evaluation, and risk/benefit analysis. It is worthy of noting that ISO 14971 deals with an as-low-as-reasonably -practicable (ALARP) approach when establishing the risk acceptability policy. After a particular risk control option has been exercised, the residual risk(s) may be in between acceptable

and unacceptable regions. For these risks, the residual risk is acceptable for the option that reduces the risk to the lowest practicable level. It may be convenient to use the ALARP approach for risks of which probability cannot be estimated. Completing the evaluation of overall residual risk acceptability, a review of the risk management process should be carried out prior to release for commercial distribution of the medical device. Schematic representation of the risk management process is depicted in Fig. 1.

3. Application to Dental Implants

The leading company of dental implant market in Korea has initiated the risk management process in cooperation with KFDA (Korea Food and Drug Administration) in 2008, and the process has been implemented for development and manufacturing of dental implants and surgical tools. Risk management for the development of newly designed implant fixture is briefly discussed in the below.

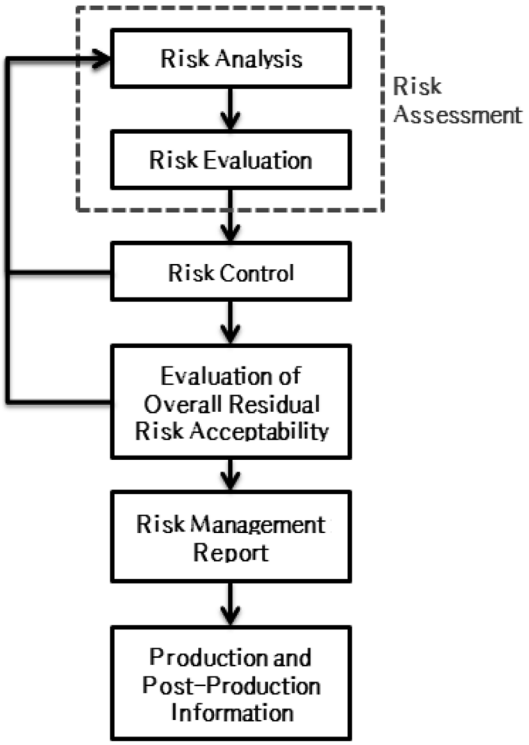

Fig. 1. Risk management process[1)]

3.1. Hazard Identification

Referring to Annexes C and E of ISO 14971, identification of intended use and characteristics related to the safety of the medical device are prepared by the risk analysis personnel. Twenty nine potential hazards have been identified as shown in Table 1. Most of the hazards are identified on the basis of clinical papers, ISO standards, and internal information on production and maintenance.

3.2. Risk Estimation and Acceptability

Referring to Annexes C and E of ISO 14971, A semi-quantitative analysis specified in D.3.4.2 of ISO 14971 has been adapted, and a 5 × 5 risk matrix is

Table 1. Hazard identification of dental implant

ID	Hazard	Hazardous Situation
R1	Design	Errors of Selecting Material
R2		Errors in the Fixture Design
R3	Diagnosis	Errors in Measuring a Bone Quality
R4		Errors of Measuring an Anatomic Structure
R5	Surgical Operation	Misrepresentation of the Specification Info.
R6		Misrepresentation of Precautions
R7		Misrepresentation of Directions
R8		Use of an Expired Product
R9		Over Torque
R10		Errors of the Insertion Depth
R11		Errors of Connecting Mounts
R12		Errors of Connecting Cover Screw
R13	Production	CNC Programming Errors
R15		Defects in Cutting Tools
R16		Out of Specification
R17		Out of Tool Holder Setting Point
R18		Cleaning Machine Stoppage
R19		Post Machine Stoppage
R20		Residual Chip and Dump
R21		Product Mixed Up
R22		Defects in Masking Jig
R23		Steam Cleaner Stoppage
R24		Dropping Product
R25		Defects in Alkali Recycling
R26		Double Marking
R27		Blister Unforming
R28		Label Information Errors
R29		Humidity Out of Specification

used. The severity levels of individual harms are determined on the basis of focused group interviews (FGIs) with expert dentists with over 10 years of experience in implant dentistry, and descriptions on each severity level are also derived from FGIs. The probability of occurrence of harms is estimated by analyzing published FDA data and internal customer complaints database. Thus the severity and probability of occurrence of harms are estimated for all harms identified. Risk acceptability criteria are indicated in a 5 × 5 risk evaluation matrix as shown in Table 2. It is noted that an ALARP approach is adapted. No harms are evaluated to be unacceptable and six harms are located in ALARP regions as shown in Table 3. Risks associated with individual harms are calculated by multiplying the severity and probability scores.

3.3. Risk Control Measures: An Example

Risk control option analysis has been performed to determine whether risk reduction is required for harms in ALARP regions, and risk control measures have been implemented for all harms in ALARP regions. Residual risk for individual harms is evaluated to be acceptable as shown in Table 4. For example, a hazard in diagnosis may lead to a hazardous situation of committing errors of measuring a bone quality, which may cause the harm of bone loss or insufficient initial stability. The severity and probability of the harm are evaluated to be 2 and 3, respectively, which results in ALARP. In this case, alleviating severity of the harm would be costly and time consuming.

Thus, risk control measures to reduce the probability of occurrence would be more practicable. One of the identified control measures to reduce the occurrence of the harm R3 is to optimize the design of surgical drills which has a significant effect on the bone loss and initial stability. A twist drill is mostly used to secure enough space at the site for an effective and safe placement of dental implants. Drilling causes a certain amount of heat around the alveolus bone, which often results in the bone loss and insufficient initial stability of implant fixtures. Thus the amount of heat generation is clearly affected by the design of surgical drills. There are many design factors affecting the performance of drills including point angle, helix angle, relief angle, flute geometry, and tip shape, among which angle-related design factors are specified based on the prior experiments. To reduce the amount of heat generated when drilling, an experiment is conducted with two design factors: flute geometry and tip shape. Four different drills areprepared to conduct a two-level factorial experiment as

Table 2. Risk evaluation matrix

Probability**	Severity*				
	1	2	3	4	5
1	ACC	ACC	ACC	ACC	ALARP
2	ACC	ACC	ALARP	ALARP	IR
3	ACC	ALARP	ALARP	IR	IR
4	ACC	ALARP	IR	IR	IR
5	ALARP	IR	IR	IR	IR

※ IR : Intolerable Region, ACC : Acceptable Region
* Severity Score: 1 (Negligible), 2 (Minor), 3 (Serious), 4 (Critical), 5 (Catastrophic)
** Probability Score: 1 (Frequent), 2 (Probable), 3 (Occasional), 4 (Remote), 5 (Improbable)

Table 3. Harms in ALARP regions

ID	Harm	Severity	Probability	Risk
R3	Bone Loss or Insufficient Initial Stability	2	3	6
R6	Inflammation Provocation & Loss of Function by Infection	5	1	5
R8	Inflammation Provocation & Failure of Osseo-Integration	5	1	5
R9	Fracture of Alveolar Bone	2	4	8
R26	Out of Specification	3	3	9
R28	Increased Bacteria	3	2	6

Table 4. Risk control measures

ID	Harm	Severity	Probability	Risk
R3	Design Optimization of Surgical Drill Providing Proper Information on Surgical Procedures	2	2	4
R6	Providing Surgical Information in User's Manual	4	1	4
R8	Expression of the Available Period in User's Manual	3	1	3
R9	Implantation Torque Test Providing Proper Information on Surgical Procedures	2	2	4
R26	Packaging IOQ Validation of Packaging Inspection Records	3	1	3
R28	Chart Record Monitoring Bioburden Test	3	1	3

given in Table 5. Changes in heat cannot be measured directly, but they may be detected their effect on the alveolus bone, i.e., changes in temperature. Drilling on artificial bone specimens with uniform density using the equipment shown in Fig. 2, five measurements of temperature are taken with respect to drilling depth.

Experimental results are summarized in Table 6 and Fig. 3, and a two-way analysis of variance (ANOVA) indicates that both factors have significant effects on changes in temperature with p-value less than 0.01 and 96.87% of R-square. Since changes in temperature are much smaller, 2-flute is preferable to 3-flute with respect to flute geometry. Further, conventional no-step drills may be replaced by step drills to reduce the changes in temperature. In conclusion, 2-flute step drill design has been adapted and deployed for further validation. Afterward, new surgical drills have been shipped out to customers and clinical data are currently stacked for updating risk management profiles. In addition to the optimization of surgical drill design, providing proper information on surgical procedures in the product catalog is also identified as a proper control measure and executing these measures is judged to reduce the occurrence level to 2. Consequently, the risk related to the harm can be reduced from 6 to 4 to be acceptable.

Table 5. Factor levels

Factor	Levels	
	Low	High
Flute Geometry	2-Flute	3-Flute
Drill Tip Shape	No-Step Drill	Step Drill

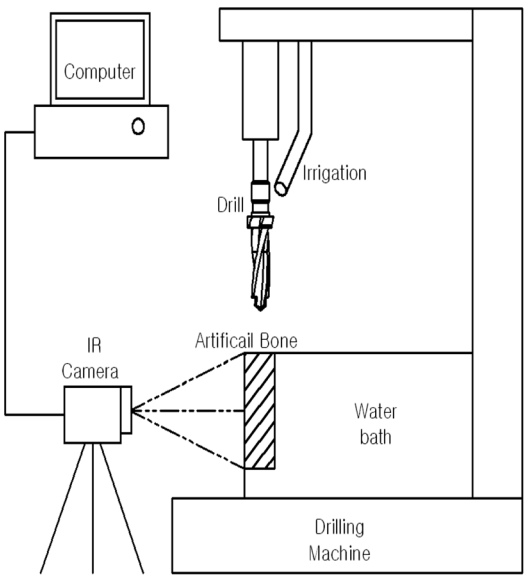

Fig. 2. Schematic diagram of experimental equipment.

Table 6. Experimental results

Type	Description	Temperature Changes
		Mean ± SD(℃)
A	3-Flute, No-Step Drill	22.72 ± 1.63
B	3-Flute, Step Drill	19.92 ± 0.82
C	2-Flute, No-Step Drill	15.10 ± 1.02
D	2-Flute, Step Drill	7.16 ± 1.15

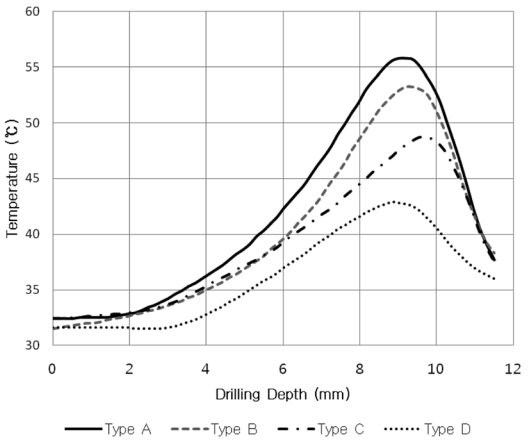

Fig. 3. Temperature changes with respect to depth.

Table 7. ANOVA Table

Sources	DF	SS	MS	F
Flute	1	559.7	559.7	392.1
Drill Tip	1	124.0	124.0	86.9
Interaction	1	23.8	23.8	16.7
Error	16	22.8	1.5	-
Total	19	730.3	-	-

※ R-square = 96.87%, R-square(adj.) = 96.29%

4. Conclusions

A proper management of risks associated with medical devices is particularly important because any single failure may result in serious damages to body or even loss of life. In this regard, the concepts of

risk management have drawn an increasing attention from the community of medical devices including medical practitioners, organizations providing health care services, governments, industry, patients and members of the public. In this study, the application of risk management to medical devices is first briefly reviewed, and the risk management process for dental implants is then investigated. Referring to ISO 14971, hazards associated with the design, diagnosis, surgical operation, and production of dental implants are identified. Risks corresponding to identified hazards are then evaluated with respect to probability and severity. Risk control measures are investigated and it has been found that conventional statistical tools such as experimental designs may be beneficial for the purpose of risk control and risk reduction in the course of development and manufacturing of medical devices.

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