

**Diplomarbeit**

**Diagnostic Value of Teledermoscopy for  
Skin Cancer Prevention**

eingereicht von  
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zur Erlangung des akademischen Grades

**Doktor(in) der gesamten Heilkunde  
(Dr. med. univ.)**

an der  
**Medizinischen Universität Graz**

ausgeführt am  
**Institut/Klinik für Dermatologie und Venerologie, LKH Graz**

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Graz, am.....

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## **Acknowledgement**

At this point, first of all I would like to say thank you to everybody who made it possible for me to study medicine at the Medical University of Graz.

Special thanks go to Prof. Dr. Rainer Hofmann-Wellenhof who oversaw my diploma thesis.

I also want to thank Dr. Julia Frühauf very much. Without her constant support and expert opinion this diploma thesis would not have been possible in this form.

I am very grateful for my family, who supported me in every way and made my education possible in the first place.

Thank you!

## Abstract

**Background:** Teledermatology (TD), a discipline of telemedicine, supplies dermatological expertise at a distance. A specific application of TD that has been repeatedly tested is the use of dermatologist-directed store-and-forward triage systems. Even with regard to skin cancer, which incidence rate is continuously increasing worldwide, TD may be a valuable triage tool for providing early diagnosis of disease, facilitating patient management and improving therapeutic decisions.

**Objective:** To evaluate the applicability of a second opinion teleconsultation service among patients attending centres for preventive health care in Austria.

**Design:** In a routine setting, general practitioners performed teledermoscopy using a digital dermoscopic system and clinical images were taken with a high-resolution digital camera. Images of suspicious skin tumours were then transmitted via virtual private network for decision-making. In cases of suspected malignancy, results were compared with a reference standard derived from histopathologic or FTF findings following referral to a local specialist. In addition, the general practitioners' acceptance of and confidence in the teleconsultation service was evaluated using a specifically developed questionnaire.

**Results:** From 2008-2010, 962 dermoscopic and 123 clinical images were obtained from 693 patients. In 122 lesions of 112 patients an excision or FTF examination by a local specialist was recommended. Diagnoses from thirty-two of these 122 lesions could be verified by histopathology (n=19) or FTF examination (n=13). In these cases, remote decisions showed a strong concordance with the reference standard (detailed diagnoses: 91.7%; tumour category: 96.9%); all malignant lesions (n=8) and 23/24 benign lesions were correctly identified (sensitivity: 100%; specificity: 95.8%). However, the GPs were only partly satisfied with the service. In particular, they expressed reservations about system usability and legal ambiguities.

**Conclusions:** A remote second-opinion service seems suitable to triage out clearly benign skin tumours, thus allowing obvious malignancies and equivocal skin lesions to be appropriately managed also by non-experts, such as general practitioners. However, besides the removal of legal ambiguities, further technical advancements seem mandatory to make the service applicable also for routine usage.

## Zusammenfassung

**Hintergrund:** Teledermatologie (TD), eine spezielle Disziplin der Telemedizin, bietet dermatologisches Fachwissen auf Distanz. Als spezielle Anwendung der TD scheint dermatologischen store-and-forward Triagesystemen ein wichtiger Stellenwert zuzukommen. Vor dem Hintergrund der weltweit steigenden Inzidenzraten, scheinen solche Triage-Systeme vor allem bei Hautkrebs sinnvoll angewendet werden zu können, um Früherkennung, Patientenmanagement und Therapieentscheidungen zu verbessern.

**Zielsetzung:** Prüfen der Anwendbarkeit von teledermatologischen second-opinion Diensten für PatientInnen, die spezielle Vorsorgezentren in Österreich aufsuchen.

**Aufbau:** AllgemeinmedizinerInnen (AM) übermittelten im Routinebetrieb dermatoskopische und klinische Bilder von suspekten Hauttumoren, die mittels eines digitalen Dermatoskopiesystems bzw. einer Digitalkamera erstellt wurden, via spezieller Internetseite zur Telekonsultation. Bei Malignitätsverdacht einer Hautläsion wurden die Telediagnosen mit einem Referenzstandard (Histologie oder Face-to-Face (FTF) Untersuchung durch einen ortsansässigen Spezialisten) verglichen. Mittels eines eigens entwickelten Fragebogen wurden zudem Akzeptanz und Vertrauen der AM in das Telekonsultationsservice evaluiert.

**Ergebnisse:** Zwischen 2008 und 2010 wurden 962 dermatoskopische und 123 klinische Aufnahmen von 693 PatientInnen mit suspekten Hauttumoren übermittelt. Bei 122 Läsionen von 112 PatientInnen wurde eine Exzision oder eine FTF-Untersuchung bei einer/m ortsansässigen Spezialistin/en empfohlen. Bei 32/122 Läsionen konnte die Telediagnose histopathologisch (n=19) oder via FTF-Untersuchung (n=13) verifiziert werden. Diese 32 Telediagnosen zeigten eine starke Konkordanz mit dem Referenzstandard (Einzeldiagnosen: 91,7%; Tumorkategorie: 96,9%); alle malignen Läsionen (n=8) und 23/24 benignen Läsionen wurden korrekt identifiziert (Sensitivität: 100%, Spezifität: 95,8%). Die Ärztezufriedenheit war eher gering; Kritikpunkte waren vor allem die zeitaufwendige Bedienung des Systems und gesetzliche Unklarheiten.

**Schlussfolgerung:** Ein Second-opinion Telekonsultationsservice scheint effektiv, um auch Nichtexperten, wie AM, eine sichere Unterscheidung zw. gut- und bösartigen Läsionen und damit ein adäquates PatientInnenmanagement zu ermöglichen. Für die Routineanwendung müssen allerdings noch technische Adaptierungen vorgenommen und die rechtliche Situation geklärt werden.

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## ***Abbreviations***

BCC	Basal Cell Carcinoma
CD	Clinical Dermatology
DSL	Digital Subscriber Line
ECG	Electro Cardiogram
FTF	Face-to-face
GP	General Practitioner
GPRS	General Packet Radio Service
GSM	Global System For Mobile Communication
ISDN	Integrated Services Digital Network
JPEG	Joint Photographic Experts Group
KB	Kilobyte
MB	Megabyte
MM	Malignant Melanoma
MP-to-MP	Medical Professional-to-Medical Professional
MP-to-P	Medical Professional-to- Patient
NMSC	Nonmelanoma Skin Cancer
NPD	Non Polarized Light Dermoscopy
PCD	Polarized Light Contact Dermoscopy
PNCD	Polarized Light Noncontact Dermoscopy
SCC	Squamous Cell Carcinoma
S&F	Store and Forward
SK	Seborrhoic keratosis
SPF	Sun Proof Factor
SSE	Skin Self Examination
TD	Teledermatology
UMTS	Universal Mobile Telecommunications System
WWW	World Wide Web
WHO	World Health Organization

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# 1. Telemedicine and Telehealth

## 1.1. General Introduction

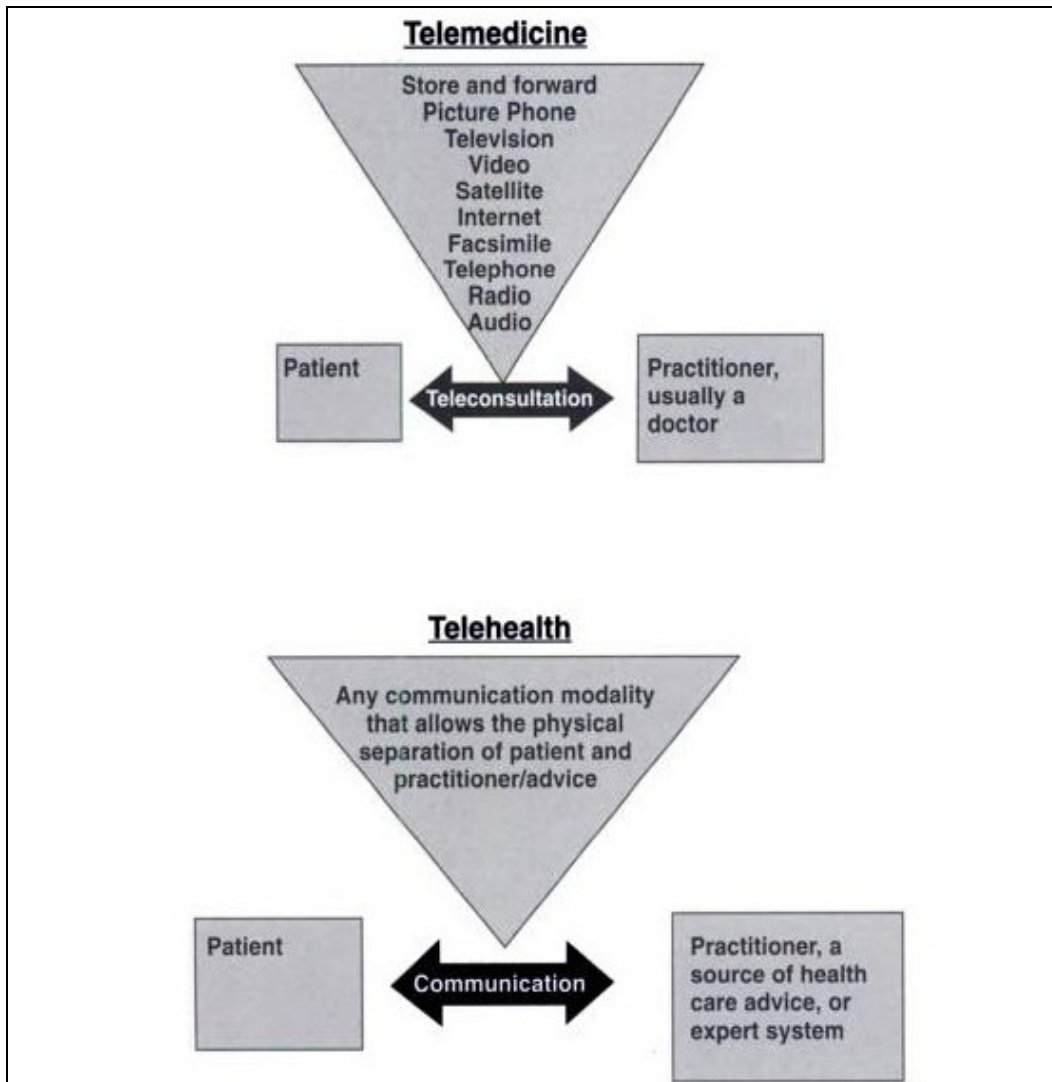
Centuries ago, medical care was only available in a certain area around a physician's working field so the distance between the patient and the doctor was crucial. The development of the World Wide Web (WWW) in the 1980s, the use of telephones and satellite communications, constituted the prerequisites to make remote healthcare delivery, also called telemedicine, possible.

The prefix „tele“ derives from the Greek for „at a distance“; hence, more simply, telemedicine is medicine at a distance. As such, it encompasses the whole range of medical activities including diagnosis, treatment and prevention of disease, continuing education of health-care providers and consumers, and research and evaluation [1].

The World Health Organization (WHO) makes a distinction between telemedicine and telehealth:

If telehealth is understood to mean the integration of telecommunications systems into the practice of protecting and promoting health, while telemedicine is the incorporation of these systems into curative medicine, then it must be acknowledged that telehealth corresponds more closely to the international activities of WHO in the field of public health. It covers education for health, public and community health, health systems development and epidemiology, whereas telemedicine is orientated more towards the clinical aspect [2].

Although there are slight differences between the two terms of telemedicine and telehealth, a lot of authors use both for the same meaning because in our healthcare system today, telemedicine is not limited to delivering curative medical treatment anymore but is also used for health promotions, disease prevention and palliative care. Figure 1.1 gives a visual impression of the definitions [2].



**Figure 1.1 Telemedicine – Telehealth illustration [2]**

Telemedicine is a fast growing and more and more important field in modern health care. In 1990, for example, it was still impossible to find even ten telemedicine programs in the United States of America; four years later, at least thirtyfive states started such programs [3].

This finding might reflect the fact that telemedicine responds quite well to today's challenges, such as growing life expectancy, increased rate of chronic diseases, decreased number of doctors and exploding health care costs.

Against the background that telemedicine is still in its beginnings, it is interesting that patients highly accept such services. A Harris interactive online survey including 2,638 American adults for the Wall Street Journal in 2005 reflects patients' opinion on telemedicine. About three quaters of the interviewees think that electronic medical records can contribute to a reduction of unnecessary tests and procedures and also significantly reduce healthcare costs. The survey shows

that four out of five patients would prefer communicating with their general practitioner online rather than visiting a medical practice. In Table 1.1 results from a survey held in 2002 are opposed to the results of 2005, the differences are only marginal [4].

	2002	2005
Ask questions where no visit is necessary	77%	80%
Fix appointments	71%	69%
Get new prescription for your medication	71%	67%
Receive results on medical tests	70%	69%

**Table 1.1 Consumer interest in online communications with general practitioners [4]**

Some skeptic may ask why telemedicine is being used at all. There might be two possible reasons: firstly, there might simply be no other alternative, such as in seafaring, aviation or astronautics [5, 6]. Or secondly, telemedicine might offer advantages compared to the conventional medical care system.

In the recent years, several studies could demonstrate that telemedicine facilitates medical support, particularly for those, who live in remote areas. Large distances and high travel costs as well as the lack of medical experts might be effectively bridged through the use of telemedicine services [7, 8]. Long waiting times and unnecessary referrals can also be reduced [9, 10]. By simplifying communication between physicians, but also between physicians and patients, also urban areas may benefit from this new mode of health care delivery. It could be shown, for example, that doctors in peripheral hospitals could improve their skills with respect to interpretation of medical findings after having received advice and counselling from a telemedicine centre [11]. Telemonitoring offers the opportunity to handle chronic diseases easier and more cost-effective, e.g. in nursing homes [12]. There are also advantages in the training and education of health-care professionals due to the facilitated and fast access to the newest medical expertise worldwide.

A problem remaining with telemedicine is that the legal situation is not totally figured out. The European Union (EU) develops new laws to regulate cross-border telemedicine in Europe. Certainly it is a difficult undertaking, because EU treaties assure every member state its independency in managing the healthcare system.

So only if the member state is not able to manage a certain issue by itself, a European-wide solution should be available.

The claim for a European-wide legislation came from the member states health ministers by the way. In 2008 the European Commission proposed a EU Directive for cross-border health care. European legislation does however not replace national health laws; it is more of an addition to it. The directive on cross-border healthcare amongst other things says that the law of the country where the patient receives the telemedicine treatment is valid and that the same professional medical- and safety standards as for conventional healthcare have to be applied for telemedicine [13]. In case of a medical mistake or dissatisfaction with the treatment, for example, the patient can sue the local healthcare provider. In the Netherlands it is already possible to sue the telemedicine provider as well. If the patient does however not have any contact with a local healthcare provider but only receives telemedicine service, it will probably be the case that the provider of the telemedicine service can be sued [13]. More precise examination of the cross-border legislation would go beyond the scope of this paper though.

In any case, professional regulations, data privacy protection and professional secrecy have to be adjusted to new circumstances. Eighty-six percent of doctors and 62% of health care providers in Germany consider the threat of violation of data privacy protection to be extensive. Nevertheless, the fear of data privacy violation does not exist under the patients [14].

## ***1.2. Modes of Data Transmission***

The modes of data transmission can broadly be classified into two main categories: store-and-forward and real-time. Store-and-forward means that data is prerecorded and transferred to another person, who can access the data at any time without the need of both sides to be online at the same time. Email is an example for this technique. This asynchronus method is most commonly used for diagnosis and for the remote monitoring of patients with chronic diseases, such as diabetes mellitus or chronic heart disease. Under the supervision of their doctors, patients are trained to check their condition by themselves, thus improving self-responsibility for their illness, which may further lead to reduced in-patient stays and health care costs.

In contrast, real-time telemedicine uses a synchronic mode of data transmission, which means that both sides need to be online at the same time. It includes all modes of real-time communication, such as phone- or video communication. This method is used for diagnosis as well as for remote monitoring and patient support. It is impossible to imagine e.g. telepsychiatry or teleemergency medicine without real-time applications.

### **Advantages and disadvantages of both methods**

Store-and-forward is a convenient method, as the management of meetings between „clients“ and „experts“ is quite easy to handle. Furthermore, lower-bandwidth connections suffice and the required equipment is rather cheap and therefore easily affordable. On the other hand real-time interactions offer the opportunity to receive immediate results to a request and to discuss medical problems in real-time. Whether to use the synchronous or asynchronous technique should be decided each time respective to the given health care scenario [15].

### **Technical details**

The types of information transferred in a telemedicine interaction, in store-and-forward as well as in real-time technique, are the following:

- Audio (i.e. the telephone)
- Text data
- Still images
- Moving images (video)

The required bandwidth is dependent on the type of information being transferred; electrocardiographic data, for example, needs low bandwidth compared to uncompressed video files, which need very high bandwidth [1].

The minimum requirement for telemedicine is an ISDN (Integrated Services Digital Network) connection, although DSL (Digital Subscriber Line) connections are recommendable. The data rate for ISDN connections depends on how many channels are used (up to 24 channels) and it can reach 1.544 Mbits/s. There are various types of DSL connections, often collectively referred to as xDSL. The

downstream rates depending on DSL version a downstream distance range from 1.544 Mbit/s to 51.84 Mbit/s [16]. For hospitals faster connections are necessary like E1 or E3, which are connection types of the E-carrier system; this is a communication system and standard defined by the European Conference of Postal and Telecommunications Administrations that provides multiplexed, multichannel, point-to-point communication links [16]. E1 offers transfer rates of 2,048 Mbit/s, and E3, which is equivalent to sixteen E1 circuits, offers a rate of 34,368 Mbit/s.

For mobile transactions GSM (Global System for Mobile Communications), GPRS (General Packet Radio Service) or UMTS (Universal Mobile Telecommunications System) can be used [17]. Table 1.2 shows some examples for required transfer rates and data sizes [18]. Regarding still image transfer that is particularly used for second-opinion teledermatology consultations, low bandwidth Internet connections are sufficient for acceptable transfer rates [19]. It is depending on image resolution of course, but with a wide spread of DSL connections nowadays, high definition images with image sizes of 3-4 MB can be transferred in just a few seconds.

<b>Digital device</b>	<b>Data rate required</b>
Digital Blood Pressure Monitor (sphygmomanometer)	< 10 kilobits of data per second (kbps) (required transmission rates)
Digital thermometer	< 10 kbps (required transmission rates)
Digital audio stethoscope and integrated electrocardiogram	<10 kbps (required transmission rates)
Ultrasound, Angiogram	256 kilobytes (KB) (image size)
Magnetic resonance image	384 KB (image size)
Scanned x-ray	1.8 megabytes (MB) (image size)
Digital radiography	6 MB (image size)
Mammogram	24 MB (image size)
Compressed and full motion video (e.g., nasopharyngoscope, ophthalmoscope, proctoscope, episcope, ENT scope)	384 kbps to 1.544 Mb/s (speed)

**Table 1.2 Data rates of typical applications [18]**

### **1.3. Fields of Application**

Telemedicine uses two main modes of interaction: the medical professional (doctor/nurse)-to-patient (MP-to-P) and the medical professional-to-medical professional (MP-to-MP) interaction.

**MP-to-P interactions** are commonly used to provide remote diagnosis, therapy, or monitoring, with the last being probably the most important aspect of MP-to-P interactions.

A practical example for **telemonitoring**, which is an application of the MP-to-P interaction as mentioned before, is the TeleUlcus project, which was carried out at the wound care center at the Department of Dermatology, Medical University Graz, Austria [20]. It was started in March 2009 with four remote hospitals (Leoben, Bruck/Mur, Mariazell and Mürzzuschlag) participating. The project's goal was to reduce outpatient visits for patients with chronic leg ulcers and to reduce travel-costs. To make this possible, specialists on wound management were introduced and could be consulted via Internet by home-care nurses, thus also increasing the medical expertise in the non-clinical field. Once a week, the home-care nurses took pictures of the ulcers and sent them together with some relevant clinical information to a wound expert via a secure internet connection. According to the expert opinion, the home-care nurses carried out the treatment at home. There were a total of 492 consultations of which in one-third (147 cases) treatment adoptions were made. The program lead to a significant decrease in outpatient visitis to general practitioners or a wound care center and 71% of the ulcers significantly improved. Furthermore, this teledermatology service was well accepted among patients, home-care nurses and participating wound experts [21].

An example for **telediagnosis** can be shown on the basis of another project carried out in Austria. During a 3-month period, 88 patients with a total of 113 skin tumors were selected in the outpatient clinic of the Department of Dermatology in Graz. A clinician took clinical and dermoscopic pictures of suspect lesions with a mobile phone camera. For dermoscopic images a dermoscope was applied to the camera lens. Both clinical and dermoscopic images were then separately

diagnosed by a teledermatologist. The results were compared to face-to-face examination and histopathology as the gold standard. The concordance rate with the gold standard was excellent (90.4%) for both clinical and dermoscopic images. Sensitivity and specificity were equal for both methods. Accuracy rates regarding detailed diagnoses were shown to be slightly higher for clinical image teleevaluation compared to teledermoscopy [22]. This and other studies showed the advantages of mobile phone based teledermatology. Using mobile camera phones at home, patients are empowered to actively take care of their own health. Furthermore, a cost- and time-saving mode of data transmission has been established [23].

In the field of dermatology, **teletherapy** still plays a minor role till date. Only few studies [24, 25, 26] have been conducted up to now, focusing on radioisotope therapy for SCC and BCC. The short-term results were comparable to standard treatment.

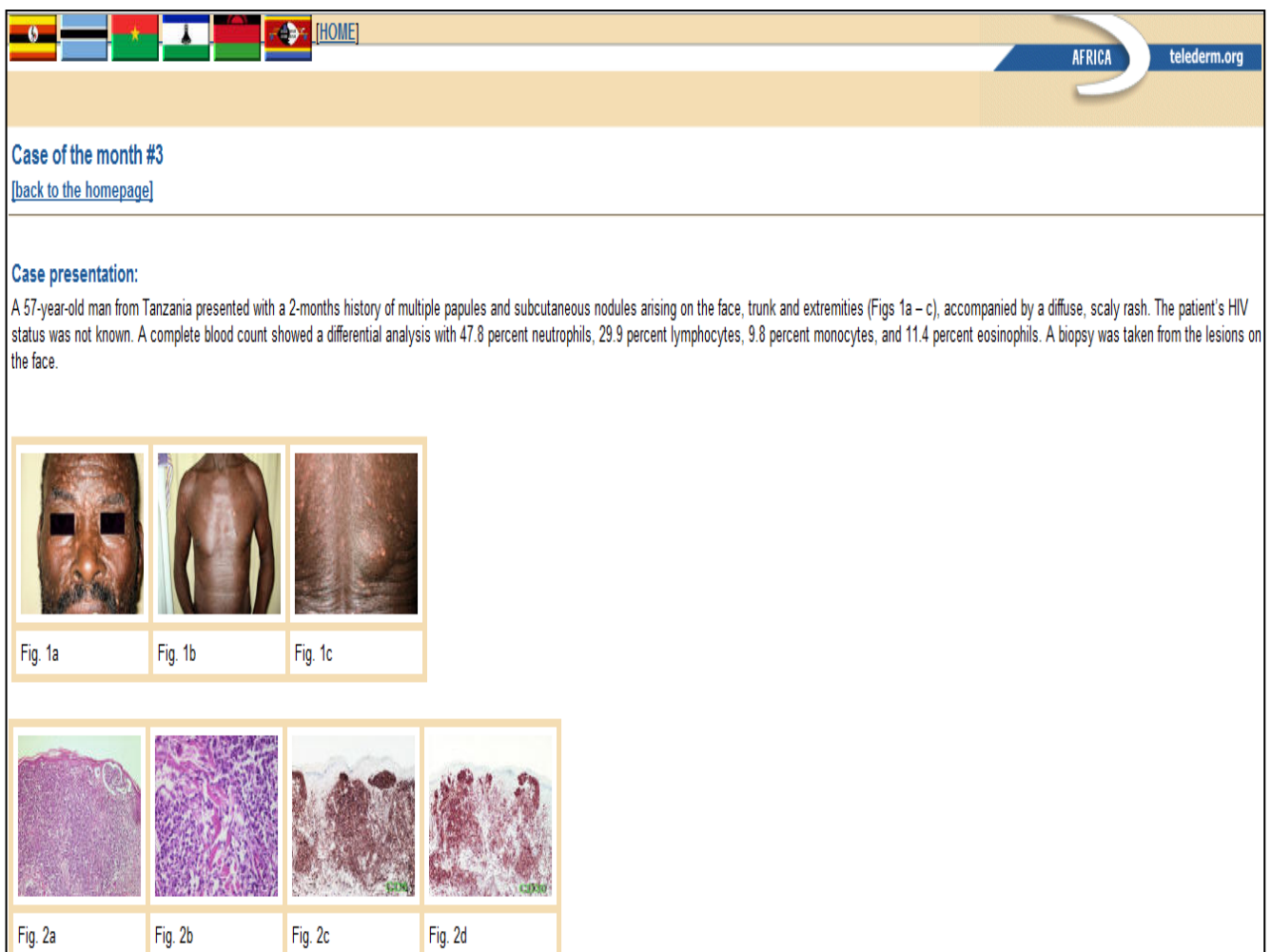
However, in Urology for example, teletherapy is being used successfully to treat prostate cancer. Eight-year survival rates ranging from 72% to 85% and ten-year survival of 62% have been shown [27, 28].

**MP-to-MP interactions** by contrast, are mainly used for second-opinion teleconsulting, as well as for educational and training purposes.

A practical example for a **second-opinion teleconsulting** service is the Africa teledermatology project, which is a cooperation of the Medical University of Graz, the University of Pennsylvania and the University of Queensland [29]. Many African countries were participating in the project, including Botswana, Eritrea, Kenya, Lesotho, Liberia, Malawi, Mozambique, Nigeria, Somalia, South Africa, Swaziland, Tanzania and Uganda. Requirements for participation in the project were the availability of special hard-, (e.g. digital cameras, computers) and software as well as sufficiently trained personnel.

African developing countries have a very limited number of physicians, in some areas as little as 10 doctors per 100,000 inhabitants and no dermatologist at all. Therefore the goal of this project was to create a network for teleconsultation and training to support local physicians in their dermatological diagnoses and treatment recommendations [30]. This virtual collaboration offered benefits not only for

African countries but also for Austria, Australia and the USA. In particular, a unique online archive of tropical skin conditions was built, which can be used for the training of dermatologists in those countries. For the project the telederm.org platform was used [31]. This is a free-access site that allows users to register as clients and upload cases that can either be transmitted to an expert of choice or can be posted for open discussion among the experts. Once a month, a very special case is posted on the website for educational purposes (Figure 1.2) [29].



**Figure 2.2 African Telederm Project – Case of the month [29]**

Moreover, a curriculum with educational material including exemplary cases with comprehensive discussions were presented on the website.

In a two year observation period between 2007 and 2009, clinicians from thirteen African nations sent consultations that were processed via the project website. The most common diagnoses included adverse drug reactions, atopic dermatitis and eczema, cutaneous infections, psoriasis and HIV/AIDS-related cutaneous

diseases [30]. After the teledermatology service had been introduced to the sub-Saharan African clinics, a significant improvement of diagnostic and therapeutic accuracy was achieved for all skin conditions [32].

With regard to the use of **telemedicine for educational and training purposes**, all, doctors, nurses, and medical students, may benefit. Such services are often performed in prerecorded form using the Internet, thus offering the opportunity to be educated at any convenient time and place [1].

A practical example for teleeducation can be pointed out at the Medical University of Graz. For years the virtual medical campus (VMC) has been used for advanced education. The VMC offers a broad online database where students can access virtual lectures, video media, and web based training (WBT). Figure 1.3 shows an example [33].



**Figure 2.3 Virtual Medical Campus – Medical University Graz: Subject: Dermatology, Virtual Microscope: Malignant Melanoma [33]**

## 2. Skin Cancer Screening

### 2.1. *Epidemiology of Skin Cancer*

Skin cancer is the most common form of cancer. In the United States, for example, one third of all malignancies are skin cancer, and one out of six Caucasians develops a form of skin cancer during his lifetime [34]. The different types of skin cancer can be grouped into two main categories: non-melanoma skin cancer (NMSC) and malignant melanoma (MM).

#### ***Non-melanoma skin cancer (NMSC):***

NMSC is the most common form of skin cancer among Caucasians [35], showing a remarkable increase in incidence over the last decades worldwide. There are two main types of NMSC: the basal cell carcinoma (BCC) and the squamous cell carcinoma (SCC).

**BCC** is more common than the SCC and often located on the head, neck or the trunk. The BCC normally grows slowly and spreads only locally. It has very little potential to metastasize (1 in 10,000 cases) [36] and in case of a low-risk lesion, it is cured by simple excision in 95 to 99 percent of the time [36].

**SCC** is the second commonest skin cancer and more dangerous than the BCC as it can spread to other parts of the body especially if the tumour is thick and is located on the scalp, ear or lip (2-6% chance of metastasis) [37]. More than half of the SCCs can be found on the patient's head or neck. However, also the hands, forearms, the upper trunk and the lower legs may be affected [37]. Actinic keratoses can be seen as early precancerous lesions, as 60% of all SCCs develop out of actinic keratoses.

Although BCC and SCC tend to assume epidemic proportions, most European states, including Austria, do not have reliable epidemiologic data, as NMSC is often not recorded in cancer registers. Aguilar Bernet et al. [38] could show that

the mean age for developing BCC is about 68 years for north and central Europeans and 66 years for Spanish people. North and central European patients showed significantly higher rates of phototypes I/II and recreational sun exposure was more common in this group. Also the number of patients with multiple BCCs was significantly higher in this group. It was shown that the predominant risk factors for BCC are age, male gender, fair skin and the socioeconomic level [38]. In Germany the age-standardized incidence rate for males, depending on the region, accounts for 24.2/100,000 people up to 63.6/100,000 people [39]. For females the incidence rates range from 20.1/100,000 people to 54/100,000 people depending on the region [39].

Interestingly, north and central Europeans show significantly more BCCs and SCCs on the trunk and the limbs than people from south Europa. This fact supports the theory that a changed habit for sun exposure changes the common localisations for NMSC [38].

It is obvious that NMSC is a disease that mostly concerns elderly people. Calculations about the European Union's population show that there will be a 22% increase of people aged 65 years and older and a 50% increase of people aged 80 years and older in a period between the year 2000 and 2015 [40]. This fact makes clear that NMSC is already and will even more be confronting Europe's health care systems with great challenges.

### ***Melanoma (MM):***

Melanoma is most commonly located on trunk, legs head and neck [36].

Although MM is not the most common type of skin cancer, it might be the most dangerous one, because of its high potential for metastasis. The risk for metastasis is depending on vertical tumor thickness stated as Breslow thickness. With Breslow thickness of <1mm, the chance for metastasis during the first 5 years of the disease is less than 10%, compared to 70% with Breslow thickness of >4mm [41]. At the time of diagnosis 8.2% of the male patients show either lymph node or distant metastasis compared to 2.8% of female patients [42]. The sites mostly affected by MM metastasis are the skin, lung, brain, liver, bone and the intestine [43].

The incidence of melanoma is increasing more than any other form of cancer, and to date, MM is the seventh most common type of cancer [44]. There is a north-to-south gradient for MM incidence with consolidating numbers in the North but rapidly increasing rates in the southern parts of Europe [45].

In Austria for example, the incidence of MM was 4.8/100,000 people in 1983, which increased to 8.3/100,000 people in the year 2007, thus resulting in 1004 new cases in 2007 [46]. The reason for this rise in incidence might be partly based on a changed lifestyle with increased excessive sun exposure [44, 47] as there is a peak of incidence in older age groups. Even individuals with high-risk phenotypes should therefore modify their recreational and overall UV exposure. However, also other factors (e.g. a special genetic predisposition) may contribute to the development of MM, as even children and adolescents may develop such malignancies [48].

## **2.2. Mortality of Skin Cancer**

The mortality from **NMSC** is rather low, as NMSC can be easily cured by surgical intervention. SCC is more aggressive than BCC and causes approximately 60% of the deaths attributed to NMSC [49].

Mortality rates for NMSC have continuously declined over the last decades worldwide, presumably because of improved secondary prevention procedures. In this context, it has to be mentioned that NMSCs often have not been recorded in skin cancer registers till date, thus, the amount of deaths attributed to NMSC may be misclassified in some way [36].

In 1968, in Central Europe (e.g. Germany) the age-standardized mortality rate for man was 0.56/100,000 people decreasing to 0.24/100,000 inhabitants in 1999. For women it was 0.42/100,000 people in 1968 and decreased to 0.11/100,000 inhabitants in 1999 [50].

Depending on country and author, the number of skin cancer deaths related to **MM** differs between 75% and 90% [34, 51]. In Austria in 1983, the mortality rate was 1.4/100,000 people for women and 2.2/100,000 people for men, causing 189 deaths this year. Compared to 1983, the mortality rates in 2008 showed only a

slight change with 1.5/100,000 people for women and 2.6/100,000 people for men [52]. Mortality rates from other European countries are listed in Table 2.1 [52].

In comparison to Europe, in the USA, melanoma showed mortality rates of 1.2/100,000 people for women and 2.4/100,000 people for men in 2005 in a comparable period. In Australia the mortality rate was 2.3/100,000 for females and 4.5/100,000 for males [52].

<b>Country/Year</b>	<b>Female (per 100,000)</b>	<b>Male (per 100,000)</b>
Slovenia (2008)	2.1	2.9
Sweden (2007)	1.9	3.0
Denmark (2006)	1.8	3.0
Switzerland (2007)	1.4	2.8
Hungary (2008)	1.4	2.5
Czech Republic (2008)	1.5	2.2
United Kingdom (2007)	1.5	2.2
Finland (2008)	1.2	2.2
Italy (2007)	1.1	1.7
Germany (2006)	1.0	1.7
France (2007)	1.0	1.7
Bulgaria (2008)	1.1	1.4
Greece (2008)	0.7	1.0

**Table 2.1 Mortality rates for Melanoma of skin for selected European countries [52]**

It is noticeable that men and older individuals have higher mortality rates than women and younger individuals. It seems that in younger populations the mortality rate has stabilized or has even begun to decline [44].

Comparing mortality rates worldwide, Eastern countries show explicitly lower rates than Western countries. For illustration see Figure 2.1 and 2.2 [53].

In Europe we can find lower mortality rates in the South with Greece having the lowest mortality rate in whole Europe [52].

It is also noteworthy that the 5-year survival rate has remarkably increased [54]. This finding might reflect the fact that high-quality screening and treatment methods are available nowadays. However, also the population's awareness

regarding melanoma might have increased, thus resulting in higher detection rates with the potential of surgical intervention in earlier stages [44].

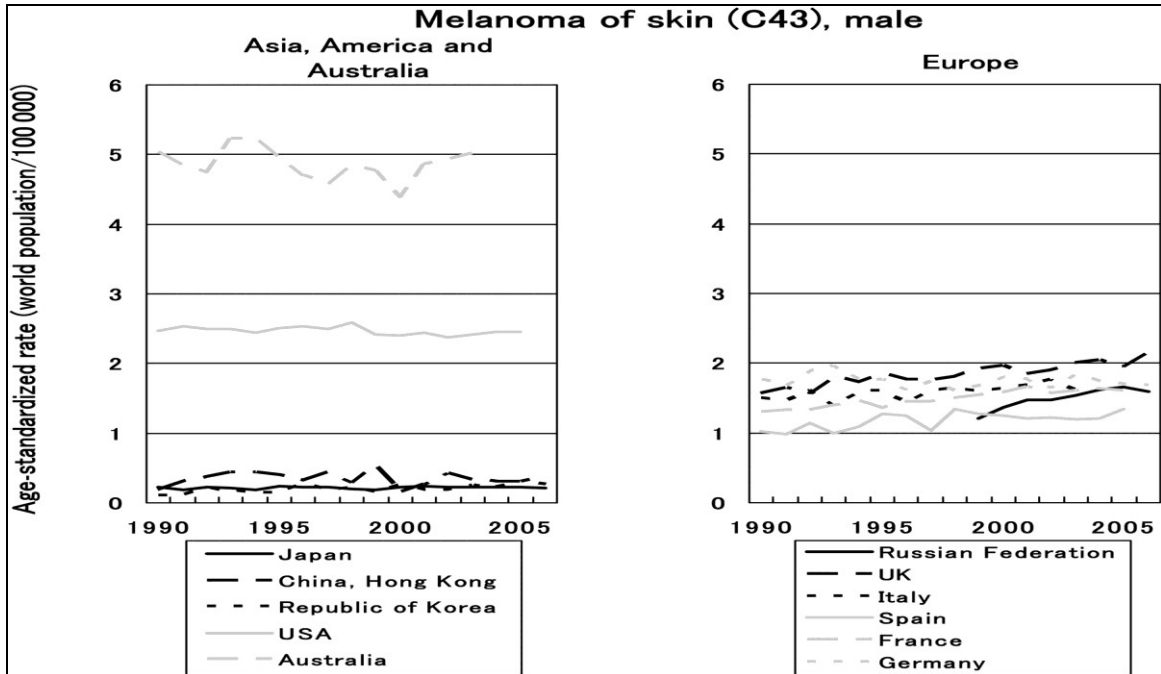


Figure 2.4 Age-standardized mortality rate for men between 1990 and 2006 [53]

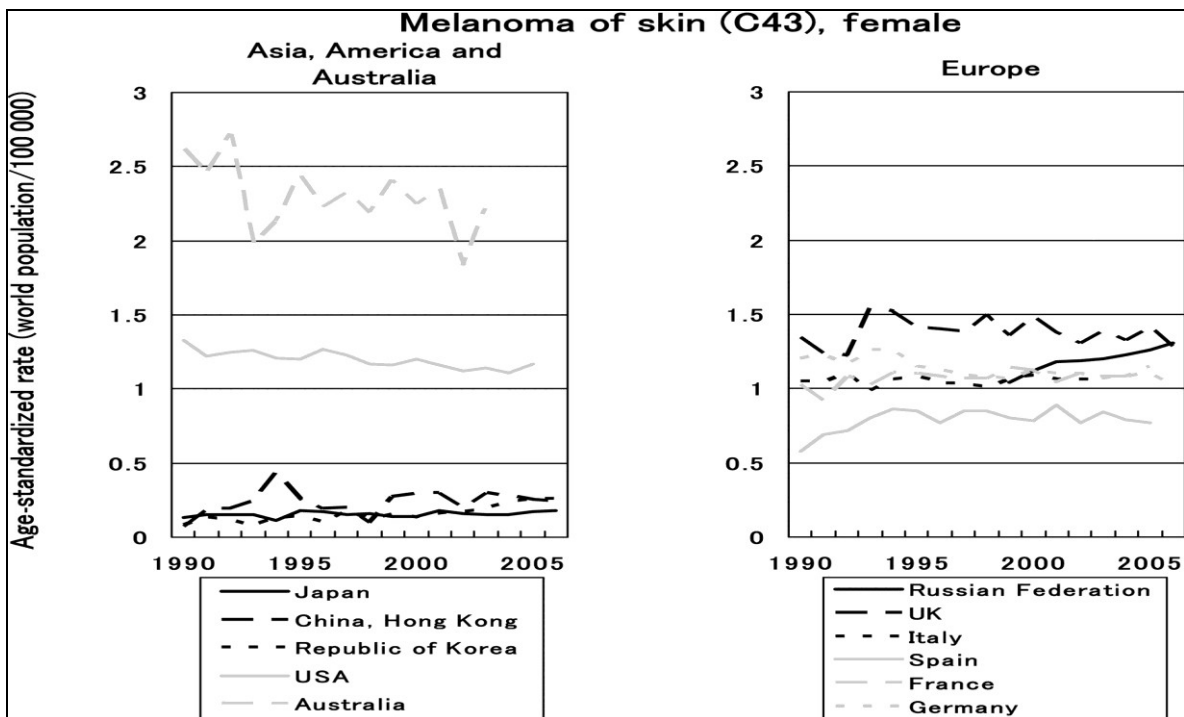


Figure 2.5 Age-standardized mortality rate for women between 1990 and 2006 [53]

### **2.3. Primary and Secondary Prevention**

The goal of primary prevention is to decrease the incidence of a disease by removing or reducing the precipitating (risk) factors which lead to the development of the disease.

In case that a disease has already occurred, it is the function of secondary prevention to detect lesions in a pre-malignant condition or early form of cancer, which may lead to timely intervention, and therefore reduced morbidity and mortality of a certain disease.

The continuous increase of incidence of skin cancer during the last decades, reflect the high perplexity of factors promoting disease initiation, thus regrettably also limiting primary prevention in this respect. On the other hand, the mortality rate did not increase equally in the same period, thus reflecting the high potential of secondary prevention programs for this disease [56].

Increased recreational sun exposure especially during childhood seems to be one major risk factor for developing melanoma as well as nonmelanoma skin cancer. The frequent use of indoor tanning, however, seems to be associated with an increased risk for developing MM, but not for NMSC [57].

Concerning **primary prevention**, the following suggestions for skin cancer prevention can be given [58]:

- a) Use sun protective agents with a factor of at least 15
- b) Wear a hat with a wide rim

It is remarkable that 76% of adults use sunscreen at least sometimes, but only a little more than half of them re-apply sufficiently [59]. Although sunscreen cannot replace other forms of sun protection, it should be constantly used in situations where clothes and other protections are not suitable [60].

In accordance to the findings of Green et al. [61] it is further recommended that high-risk patients should always use sunscreen when being outside in sunny climates. In particular, Green et al. performed a follow-up on more than one and a half thousand adults in Queensland, Australia, which is an area with one of the highest incidence rates for malignant melanoma in the world. The results of this

study showed a 50% hazard reduction for malignant melanoma for the "sunscreen-group" and even a 73% hazard reduction for preinvasive melanoma. Also the incidence rate and total number of SCC were lower (-35% respectively -38%) in the "sunscreen-group". Yet this is the first and only study so far that shows strong evidence for a reduction of malignant melanoma incidence rate after daily sunscreen use in adults [62]. With regard to NMSC, the present data suggests that regular sunscreen use may only prevent SCC but not BCC [57, 61].

A recent German study suggested that increased use of sun protection among children during summer holidays may reduce the manifestation of melanocytic nevi and therefore, also the number of resulting MM [66]. This finding was confirmed by a recent Canadian study, which demonstrated a decreased incidence of melanocytic nevi in children, particularly on intermittently sun exposed areas of the body, after a three-year use of sun protection with sun proof factor (SPF) 30+ [64]. In contrary, however, another study conducted in Australia could not find significant correlations between the use of sun protection and decreased nevi count [65].

A practical example for skin cancer prevention can be found in Greece. Since the year 2000 the Hellenic Society of Dermatology and Venereology (HSDV) runs a preventive program for MM offering free of charge public examination by dermatologists all over Greece, by providing an open MM information telephone line; brochures and TV broadcasting on the matter for a whole month; a media and press interview of HSDV board; educational programs delivered by experts and the help of teachers in elementary and high-schools. It is too early to get conclusive results for primary prevention in Greece but it seems as if secondary prevention would be successful because 50% of the detected MMs were less than 1 mm thin, which is an early stage of the disease [66]. A comparable preventive program started in Australia in the 1980s showed encouraging results with a decrease of mortality from MM at the ages beyond 55 years, a finding, which reflects the growing awareness of young people. There was no change in mortality in the group of people between 56 and 79 years and a slight increase in the group of patients with 80 years and more [67].

Key to a successful **secondary prevention** seems to be based on effective self-examination procedures for which a broad public education is necessary.

For clinical diagnosis of MM Rigel et al. [56] introduced a simple examination-rule, also called ABCD rule, which stands for asymmetry (A), border irregularity (B), colour variegation (C), and diameter more than 5 mm (D) [56]. Figure 2.1 gives a visual impression of the concept.



**Figure 2.6. The ABCD concept [68]**

The ABCD rule has recently been adjusted to the ABCDE rule, which also focuses on a recent evolution or elevation of a lesion (E) [56].

The ACBDE rule seems suitable for dermatologists in clinical use, whereas for patient self-examination purposes, the awareness of a border irregularity and a recent change of a lesion might be more expedient [69].

A study showed that the ABCDE concept, applied by experienced clinicians showed sensitivity rates ranging from 92 to 100% and specificity rates of 98% for the detection of MM [70].

Besides from skin self examination, screenings help to detect skin cancer in early stages. In the US for example the American Academy for Dermatology (AAD) offers a mass screening once a year on “Melanoma Monday” when every citizen can be checked out. Analyzes about the screening performed on 362,804 patients between 2001 and 2005 found a high-risk type of patient. It can be remembered under the acronym HARMM, standing for:

H: history of previous melanoma

A: age over 50

R: regular dermatologist absent

M: mole changing

M: male gender

High-risk patients (four or five factors positive) accounted for 5.8% of total population but 13.6% of presumptive melanoma cases were found in this group [71].

Cost analyses by Losina et al. [72] show that a one-time melanoma screening in the US population for people older than fifty years as well as a screening for siblings of melanoma patients (because of increased risk) every other year is cost-effective. The authors also point out the cost-effectiveness of a melanoma screening is comparable to screenings for breast, cervical or colorectal cancer [72].

In Germany every person aged 35 years and older has the chance to have a free whole-of skin examination every two years. An evaluation of a screening program in Bavaria including more than 100,000 people however showed that almost twenty percent of the patients suffering from malignant melanoma were younger than 35 years. The study showed that the risk factor model of the AAD was also valid here [73].

Study results indicate that it is more reasonable to concentrate on risk groups when screening for skin malignancies. It has been shown that mass screening is able to detect melanoma at an earlier stage compared to patients self-examination but regarding the survival benefit, there is no consensus if it makes a difference though [74, 75].

Jackson et al. [76] identified another risk score (MacKie score) that patients themselves can easily apply. Freckling, more than 20 common moles, atypical moles and a history of severe sunburn are the important factors of the MacKie score. According to it, 4.3% of the population are in the highest and 4.4% in the second highest risk group [76].

It should be noted that these risk group scores all account for high risk patients only. As seen before in the study held in America, 13.6% of the patients suffering from MM were in high-risk groups. So the majority of melanoma cases can not be attached to a high risk group. This circumstance somehow puts these risk scores in question. For that reason Guther et al. [73] developed a new risk group model with a high sensitivity for MM and SCC (>92%) and good overall specificity that captures the majority of skin cancer cases. Screening is recommended from the age of twenty years and the authors estimate that one third of the population can

be identified to be at risk for developing melanoma and therefore be recommended to have dermatologic examinations on a regular basis [73].

Regarding NMSC, patients should be aware of and focus on the following signs of a potentially evolving lesion:

- Nonhealing sore or ulcer
- Scaling pink or red patch not responsive to topical treatment  
Enlarging pink papule or nodule, with or without scaling, erosion, ulceration, or crusting
- Pearly papule with overlying telangiectasis, with or without scaling, erosion, ulceration, or crusting [77]

Nowadays, specialists achieve sensitivity rates between 56% and 90% and specificity rates between 75% and 90% for the clinical diagnosis of NMSC [78].

Higher diagnostic accuracy rates can be achieved when dermoscopy is used as an adjunct in the diagnostic procedure.

Dermoscopy (epiluminescence microscopy) is a noninvasive in vivo diagnostic technique that magnifies skin and reduces skin surface light reflection, allowing better visualization of structures present below the skin surface, such as melanin and blood vessels [79, 80]. Dermoscopy can be used for almost any skin lesion but is particularly applicable for the examination of moles and other pigmented skin lesions. It allows for more accurate clinical diagnoses and is an especially important tool on the early diagnosis of melanoma. Sensitivity rates for detection of MM with dermoscopy range from 0.68 to 0.96 compared to unaided eye rates of 0.42 to 0.94. Specificity ranges from 0.58 to 1.00 with dermoscopy respectively from 0.54 to 0.99 with the unaided eye [81]. It may also obviate the need for unnecessary skin biopsies and excisions. The role of dermoscopy for BCC and NMSC in general, has been investigated more extensively only recently, but is also showing promising results [78].

### **Physical fundamentals**

When light hits the skin it is reflected by the stratum corneum, dispersed, or absorbed. Naturally most of the light is reflected because of the higher refractive

index of the stratum corneum (about 1.55) compared to that of air (1.0). The reflection of the light depends on the surface of the skin. If the surface is rather regular, more light can penetrate it, if it is irregularly shaped, more light is reflected. To take advantage of this situation, for immersion contact dermoscopy a glass plate is being pushed onto the skin surface. Between the stratum corneum and the glass plate a linking fluid is used to optically link the two and thereby decreasing reflection and refraction. As linking fluids a broad spectrum of fluids can be utilized. Immersion oil shows the best results for dermoscopy but also olive oil, mineral oil, water-soluble gels (e.g. ultrasound gel) and also disinfectant solutions are useable. Because of the similar refractive indexes of the glass plate (about 1.52) and the stratum corneum an assessment of epidermal and upper reticular dermal structures is possible. In contrast to immersion contact dermoscopy where nonpolarized light is used, in recent years a new kind of dermoscope that uses polarized light was developed. The polarized dermoscopes can be used with or without a liquid interface and direct skin contact. These polarized dermoscopes work with two polarizers; a source polarizer emits unidirectional light that will be rejected by the detector polarizer. Only if the light changes its polarization it will go through the detector polarizer. When polarized light strikes the skin surface it is reflected without changing its original polarization. However when penetrating the skin it scatters and after about ten scattering events its polarization is randomized. The depth of penetration for this physical phenomenon to happen is about 60-100 micrometers. So most of the light one can see when performing dermoscopy with a polarized light dermoscope comes from deeper layers because the detector polarizer will reject singly backscattered and surface-reflected light. In a nutshell it can be said that a nonpolarized dermoscope is more convenient to examine superficial skin layers, polarized dermoscopes on the other hand allow better examination of deeper skin structures [80, 82, 83, 84].

### **The different types – which one should be used?**

All three types, nonpolarized light dermoscopy (NPD), polarized light contact dermoscopy (PCD) and polarized light noncontact dermoscopy (PNCD) generate more or less the same image quality.

As mentioned before, NPD seems to yield better results when evaluating superficial layers of the skin while PCD should be the method of choice for examination of deeper skin layers. Blood vessels for example are best visualized by PNCD, which makes it better suited for analyzing malignancies. Seborrheic keratosis (SK) can be more easily diagnosed if NPD is used because milialike cysts and comedolike openings can be recognized better [80]. Wang et al. [88] found similar results in their study, suggesting that PCD yields better results for melanoma diagnostics, while NPD should be preferred for SK [88]. In Table 2.1 Benvenuto-Andrade et al. [80] show the different capabilities of visualization for different colors and structures for all three dermatoscopy methods.

	NPD	PCD	PCND
<b>Colors</b>			
Melanin pigment	+	++	++
Red or pink	+	++	++++
Blue-white	+++	++	+
<b>Structures</b>			
Peppering	+++	++	+
Shiny-white streaks	+/-	+++	++
Blood vessels	+	++	++++
Milialike cysts and comedolike openings	++++	+/-	+/-

**Table 2.2 Different dermoscopy methods. The amount of + indicates how well a feature can be seen using a particular method. +/- means that the structure can be seen sometimes [80].**

## **3. Tele dermatology**

### **3.1. General Introduction**

In 1995, Peredenia and Brown firstly introduced the term "tele dermatology" [89]. Tele dermatology is a subcategory of telemedicine, and as such it offers remote access to expert dermatologists at almost any place and time. As dermatology is a visual discipline, it seems especially suitable for telemedicine purposes.

#### **Why do we need tele dermatology?**

More than fifteen percent of the population live in remote areas, and they have to undergo long and expensive travels in order to get specialized dermatologic care, as local general practitioners often do not have enough expertise to diagnose and treat certain skin diseases, such as skin tumours, adequately [87].

Other than the problem of accumulation of dermatologists around urban centres, there is an evident shortage of dermatological expertise among the dermatologists themselves. A survey by the American Academy of Dermatology showed that almost one third of dermatologists spent half or more time only on surgery and cosmetics [88], for which they received high compensation, thus creating a gap between dermatological supply and demand, which non-specialists such as general practitioners have to bridge [89]. However, this problem might not be solely solved by the use of tele dermatology, but potentially, by an adopted compensation system.

Tele dermatology, however, might serve as a valuable tool to compensate long waiting times for appointments and treatment, and might therefore contribute to an improvement of secondary prevention.

For conventional dermatology the average time for initial consult completion was shown to be 48 days compared to 4 days for tele dermatology [9]. Regarding the time until biopsy was performed, the delay was 57 days for conventional dermatology compared to 38 days for tele dermatology and the delay until surgery was 125 versus 104 days [9].

On average, patients, for whom a face-to-face consultation was mandatory after a teledermatological consultation, the average time until then was 12 days. In contrast, for conventional referrals it took on average 88 days. In the study more than 2000 patients participated and it was shown that in more than half of the cases a teledermatological consultation could avoid a dermatological face-to-face visit [10].

### **Quality of teledermatological care**

Recently, Warsaw et al. [3] defined criteria for the evaluation of the quality of teledermatology care. For this, they analysed 85 articles, which were published in the years 1999 to 2009.

In their review, they pointed out the following main criteria:

- Diagnostic accuracy [agreement between telediagnosis and histopathology]

Warsaw et al. [3] could demonstrate that two thirds of studies found higher diagnostic accuracy for in-person dermatology compared to teledermatology, with a mean difference in diagnostic accuracy of 5% for pigmented skin lesions and 11% for a primary diagnosis of various skin diseases in general. The diagnostic accuracy for pigmented skin lesions increased when teledermoscopy was integrated into the diagnostic procedure. Depending on the author and on the experience respectively the dermoscopy skill, the absolute difference was between 15 to 49% and even equally high accuracy rates as conventional dermatologic care could be achieved [3, 81].

- Diagnostic concordance [interobserver agreement]

Aggregated concordance rates were calculated for eight studies dealing with pigmented and nonpigmented skin lesions, showing a complete agreement of 64% between TD and clinical dermatology (CD). Also another study by Whited et al. [90] could show that interobserver agreement between TD and CD was very high.

- Management accuracy and concordance

The overall management accuracy for skin cancer has been shown to be quite equal between teledermatology and clinical dermatology, although teledermatology might be inferior for management decisions regarding malignant and premalignant skin tumours [93, 94]. With regard to triage decisions such as “refer or not refer” and “biopsy or no biopsy”, the aggregated concordance rates were good (75%) to excellent (98,5%) [3].

- Clinical outcomes [e.g. clinical course, time to treatment]

Existing data suggests that TD results in equal clinical outcomes as CD, but may fasten a patient’s recovery time [91, 92, 93]. The time to get a dermatologist’s professional opinion after seeing a GP is significantly shorter with TD as well as the time to receive definite treatment [10, 94, 95]. Depending on the study, 12.8% to 72% of the in-person visits to a dermatology clinic can be avoided with TD consultations [92, 96, 97].

- Patient and physician acceptance

Whited et al. [98] could show that the majority of referring primary-care physicians favored teledermatology consultations over usual care. 92% of the physicians were satisfied with the teledermatology consult process. The reasons mentioned were more timely appointments for patients and a better educational benefit with TD consultations. Seventy-five percent of consulting dermatologists were overall satisfied with TD. All dermatologists agreed that TD is an easier approach for triage of patients compared to clinical appointments. Patient satisfaction was high for both TD and conventional care. The most frequently voiced point of objection in patients was the long waiting times under conventional care. TD patients on the other hand criticized that they had not been informed about the results of the teleconsultations quick enough. All in all 41% of the patients favored a TD consultation, 36% preferred usual care and the rest was indecisive [98].

- Costs

There are many factors that have to be considered. However, in general, it can be said that teledermatology is more cost effective than conventional care, if certain assumed parameters like patient travel distance, loss of productivity, and costs of clinical dermatology and volume of teledermatology were met [3, 99].

### **3.2. *Clinical Image Tele-Evaluation***

Almost any teledermatological consultation contains a clinical image. It is quite simple and cheap to obtain such visual information. No more than a digital camera is needed and even a mobile camera phone suffices. Using a mobile camera phone, patients are able to take pictures of their skin tumours and send them directly to their doctor without the need of a computer. A swiss study analyzing the quality of pictures taken by patients themselves shows that the majority of pictures were adequate for decision-making. In the majority of cases it was possible to make a diagnosis based on the transmitted pictures and the clinical history. Using this approach, it is possible to decide whether the patient has to see a specialist (in case of urgency) or if he can be managed by teledermatology without having him to see a doctor in person [100].

### **3.3. *Teledermoscopy***

The diagnostic accuracy for skin tumours, particularly malignant melanoma using no other adjuvant than one's eyes is rather low showing values about 60% [81]. This finding may be similar when using teledermatology for the diagnostic procedure. Besides the fact that a clinical image may be useful in giving a general view of the affected body site, thus giving the teledermatologist the opportunity to identify other suspect lesions, the photographer has not recognized so far, it has been therefore recommended to acquire both a clinical and a dermoscopic image for remote decision-making in order to achieve optimal accuracy rates [101]. To acquire dermoscopic images, the use of standard pocket dermoscopy devices, most of which use the polarized light noncontact dermoscopy method, together

with a digital camera or a mobile phone camera may suffice for decision-making [22, 23, 102]. However, the highest image quality might be achieved using digital imaging systems, most of which incorporate a contact immersion or noncontact dermoscopy system. Digital dermoscopy is more and more used for storage and retrieval of images and thus it is very beneficial for the follow-up of pigmented skin lesions and furthermore, to easily obtain an expert opinion on difficult cases with uncertain diagnoses [103].

### **3.4. Special Application - Skin Cancer Screening**

With regard to the increasing incidence of malignant melanoma, basal cell carcinoma and squamous cell carcinoma all around the world, skin cancer screening is an important tool for detecting those lesions in an early stage of the disease.

There are two categories of screenings: on the one hand there is a screening for special risk groups and on the other hand there is a mass screening where everybody is examined. An effective mass screening should meet the following criteria: it has to be safe and accepted by the public, it should have high sensitivity and specificity rates and of course it should not be too expensive. A screening like this also holds negative aspects like an increase in unnecessary interventions, increased anxiety among the population as well as false reassurance and a disruption of routine service [104].

Oliveria et al. [105] showed that four out of five dermatologists routinely screen for skin cancer. Compared to that only half of general practitioners and internists screen their high-risk patients. The reasons given for that are time constraints and competing comorbidities [105]. Teledermatology can be a suitable alternative here and it has been proven to be an effective tool for skin cancer screening. It showed agreement rates with histopathology for the primary diagnosis of pigmented skin lesions ranging from 65% to 94% [10, 106, 107, 108, 109]. Compared to that, the agreement of clinical dermatology showed results ranging from 76% to 92% [106, 108, 109].

Moreno-Ramirez et al. [10] conducted the largest study on this topic evaluating more than 2000 patients in Spain. In this study an excellent sensitivity of 99% and a specificity of 62% could be achieved when using teledermatology for the diagnosis of skin tumours.

A key aspect in skin cancer screening is public awareness. Berwick et al. [110] suggested that through precise skin self-examination a reduction of MM mortality of 63% might be possible. Self-detection rates range from 40 to 55% depending on the study [111]. Considering that, even mobile teledermatology seems to be a favourable tool for skin cancer screening. Patients could take pictures of suspect or evolving skin lesions with their mobile phone by themselves and send the data directly to their doctor at any time and place.

Earlier studies on the feasibility of mobile teledermatology were limited by image quality due to inferior technical equipment [112].

In more recent studies however, image quality was no limiting factor anymore and very promising results using mobile TD for skin cancer screening were shown [22, 23, 102]. Besides the improvement of technical equipment, however, it has been shown that a correct TD diagnosis depends more on the diagnostic difficulty of a lesion than on the slight difference between excellent or good image quality [106], and that clinical information attached to the photographs significantly improves diagnostic accuracy for remote decisions [113].

Massone et al. [102] used mobile phone cameras with a pocket dermoscopic device for the image acquisition of skin tumours (Figure 3.1). Clinical and dermoscopic images were uploaded in JPEG (a compression format for digital images by the Joint Photographic Experts Group) format to be analyzed by two specialists. Compared to face-to-face decisions, remote diagnoses reached a diagnostic agreement of 89% when using clinical pictures only for decision-making, but 91.5% when using both image types.



**Figure 3.1 Skin cancer screening with a standard mobile phone camera and a pocket dermoscopy device [102]**

The initiation of digital dermoscopy systems such as DB-DM-MIPS System (Biomips Engineering, S.R.L., Siena, Italy) or FotoFinder System (FotoFinder Systems GmbH, Bad Birnbach, Germany), allowed an even more thorough analysis of suspect skin lesions. The dermoscopic images are acquired with a high-definition camera and automatically processed and the included software evaluates certain criteria such as diameter, color or symmetry of the lesion in real-time. Several studies could demonstrate the equality of dermoscopy and digital dermoscopy systems [114, 115, 116]. Sensitivity ranged from 90 to 95%, specificity from 79.6 to 93.3% [114, 115]. Digital dermoscopy analysis, however may prove beneficial in improving the quality of skin cancer screening by visualization of slight morphological changes that otherwise would not be recognized.

## **4. A Clinical Study**


### **4.1. Introduction**

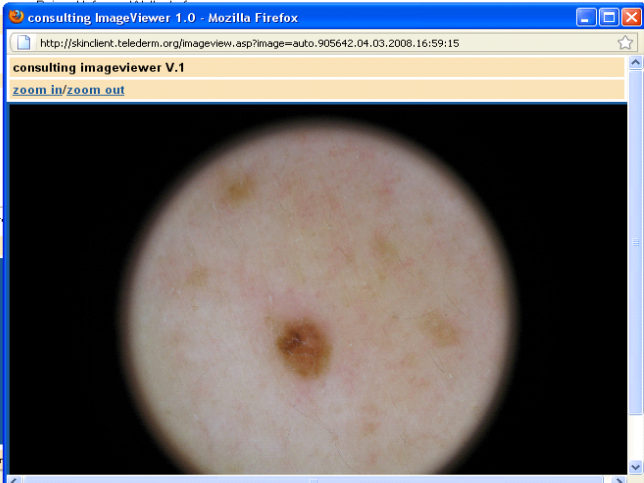
In previous studies, it has been shown that the diagnostic accuracy of teledermatology is comparable to that of face-to-face consultations [90, 106], and moreover, that teledermatology is a suitable tool for dermatologist-directed triage systems [10, 107, 112, 113].

As most of these studies were based on an artificial study design [90, 96, 106, 108, 109, 112, 113], a store-and-forward teledermatology triage system aimed at the selection of patients with skin growths suggestive of cancer was implemented at our skin clinic; the present study describes the results of the implemented TD triage system in terms of diagnostic accuracy, system usability, and GPs' acceptance of and confidence in the service.

### **4.2. Materials and Methods**

From February 2008 to February 2010, patients attending selected preventive health care centers for skin cancer screening in Austria, were selected by general practitioners (GP) for second-opinion teleconsulting because of an equivocal skin lesion. For this purpose, the GPs took at least one dermoscopic and occasionally, one clinical image of a given skin lesion. Clinical images were acquired with a Canon Powershot digital camera (Canon Inc., Tokyo, Japan) and dermoscopic pictures were obtained by using a polarized light contact dermoscope (DermLite Photo, 3Gen LLC, San Juan Capistrano, USA) that was adjusted from MoleMax System (Derma Medical Systems, Vienna, Austria). Patient data together with a short medical history were then transferred via a virtual private network (skinclient.telederm.org, e-derm-consult GmbH, Graz, Austria) to two dermoscopic experts (R.H-W, Medical University of Graz; H-P.S, School of Medicine, University of Queensland) for decision-making. Figure 4.1 shows an exemplary case.

<b>title of request</b>	user07
<b>age</b>	40 years
<b>location</b>	paravertebral, thorakal, rechts
<b>clinical history</b>	sehr viele Muttermale am ganzen Körper, heller Hauttyp Image1 recorded on 04.03.2008
<b>diagnosis</b>	Diagnosis Pending
<b>question</b>	<b>Sg Herr Prof. Hofmann, zur Begutachtung zweier weiterer Bilder ein und des selbigen Patienten, vielen Dank im vorhinein,</b>
<b>answer</b>	Hofmann-Wellenhof Rainer: Sehr geehrter Frau Kollegin Proll!  Diagnose: atypischer Naevus mit exzentrischer Hyperpigmentierung Procedere: Kontrolle in 3 Monaten Bildqualität: gut (beide Bilder)  Hier handelt es sich wiederum um einen atypischen Naevus. Die engmaschige Kontrolle würde ich durchführen, da zwischen 9 und 12 könnte. Mit freundlichen Grüßen
<b>options</b>	
<b>preferred date for the answer</b>	
<b>expert</b>	
<b>Scores</b>	
<b>Non Melanocytic</b>	
<b>3-Point</b>	
<b>ABCD</b>	
<b>7-Point</b>	
<b>Suggestion:</b>	
<b>ICD:</b>	
request type: moleexpert, id: 422, status: 4, v.1, request created: 3/4/2008 4:59:01 PM / pr	
<b>image selection</b>	
	
admin:daki95@gmx.net session 826464227 from 84.119.34.107, at 'requestdetail', ser	
Done	

**Figure 4.1** Skinclient.telederm.org, case example: note the short clinical background and patient's age on top and the dermoscopic image (also enlarged) and the clinical image

Image quality of dermoscopic and/or clinical pictures was assessed using a 3-point scale ranging from 1, excellent, to 3, low image quality.

For diagnosis, the lesions were grouped into 4 diagnostic categories (benign melanocytic, malignant melanocytic, benign non-melanocytic, and malignant non-melanocytic skin lesions). Detailed diagnoses of each category were further classified according to WHO recommendations [118] as shown in Table 4.1.

Based on these classifications, the teledermatologists recorded their diagnosis. To evaluate tele-diagnostic confidence, tele-diagnoses were correlated with a given treatment plan, such as 1) no further treatment or follow-up in a 3-, 6- or 12-month interval in case of benign skin lesions, 2) referral to a local specialist in case of suspicious skin lesions, and 3) excision in case of suspected malignancy. To assess diagnostic accuracy in case of suspicious lesions or lesions with suspected malignancy, remote diagnoses were then compared with a reference standard derived from histopathologic or face-to-face results following referral to a local specialist. Further statistical analysis aimed at assessing the sensitivity and specificity of remote diagnoses. For this purpose the true positive (TP), false positive (FP), true negative (TN) and false negative (FN) values were calculated (sensitivity:  $TP/TP+FN$ ; specificity:  $TN/TN+FP$ ).

GPs' acceptance was evaluated via questionnaires including questions about system usability (e.g.: Is the service time-consuming? Are there problems obtaining constantly good dermoscopic/clinical image quality?), and GPs' acceptance of and confidence in the teleconsultation service (e.g.: Do you feel confident with the teleconsultation service? What would you do in case of an uncertain diagnosis without telemedical supervision? Was the time for remote decisions too long? Are you satisfied with the quality of teleconsultation? Did the teleconsultation service improve the patient management? Did the teleconsultation facilitate your treatment decisions? Did you adhere to the remote recommendations? Could you imagine using the teleconsultation service in your own office?). Further, the GPs opinion was recorded regarding potential future system advancements.

### **4.3. Results**

Seven centres for preventive health care submitted 693 patients (median age: 47 years, range: 18 – 84 years), 223 of who presented with double or multiple lesions, with 962 dermoscopic and 123 clinical images for teleconsultation. Of the images taken, 89% dermoscopic versus 77% clinical images were of excellent, 10% versus 19% of moderate, and 1% versus 4% of low image quality. No definite remote diagnosis could be established in 3 cases due to low dermoscopic image quality. Four cases were diagnosed as non-tumorous, inflammatory skin lesions and were therefore excluded from analysis. The remaining 955 lesions were diagnosed by the two teledermatologists as follows: 743 benign melanocytic, 6 malignant melanocytic, 186 benign non-melanocytic, and 20 malignant non-melanocytic skin tumours (Table 4.1); There was a tendency to excise (n=112) or follow-up lesions, e.g. in a 3-month (n=49), 6-month (n=265) or a 12-months (n=393) interval; in 10 cases, referral to a specialist doctor for FTF examination was recommended; in 126 cases, no further treatment was indicated. The frequency of telediagnoses and resulting recommendations are shown in Table 4.1.

TD Diagnosis	n	Remote recommendations					
		n (%)					
		Excision	Referral	Follow-up			No treatment
				3 months	6 months	12 months	
<b>Benign melanocytic</b>							
Dysplastic nevus	503	68 (13.5)	2 (0.4)	39 (7.8)	202 (40.2)	192 (38.2)	0 (0)
Nevus	240	0 (0)	0 (0)	6 (2.5)	48 (20.0)	174 (72.5)	12 (5.0)
<b>Total</b>	<b>743</b>	<b>68 (9.2)</b>	<b>2 (0.3)</b>	<b>45 (6.1)</b>	<b>250 (33.6)</b>	<b>366 (49.3)</b>	<b>12 (1.6)</b>
<b>Malignant melanocytic</b>							
Melanoma	6	6 (100)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
<b>Total</b>	<b>6</b>	<b>6 (100)</b>	<b>0 (0)</b>	<b>0 (0)</b>	<b>0 (0)</b>	<b>0 (0)</b>	<b>0 (0)</b>
<b>Benign non-melanocytic</b>							
Seborrheic keratosis	131	16 (12.2)	1 (0.8)	2 (1.5)	4 (3.1)	15 (11.5)	93 (71.0)
Dermatofibroma	20	1 (5)	1 (5)	1 (5)	4 (20)	5 (25)	8 (40)
Solar lentigo	16	0 (0)	0 (0)	1 (6.3)	7 (43.8)	7 (43.8)	1 (6.3)
Angioma	14	1 (7.1)	2 (14.3)	0 (0)	0 (0)	0 (0)	11 (84.6)
Hemorrhage	4	0 (0)	2 (50)	0 (0)	0 (0)	0 (0)	2 (50)
Porokeratosis	1	1 (100)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
<b>Total</b>	<b>186</b>	<b>19 (10.2)</b>	<b>6 (3.2)</b>	<b>4 (2.2)</b>	<b>15 (8.1)</b>	<b>27 (14.5)</b>	<b>115 (61.8)</b>
<b>Malignant non-melanocytic</b>							
Basal cell carcinoma	15	14 (93)	1 (7)	0 (0)	0 (0)	0 (0)	0 (0)
Actinic keratosis	4	3 (75)	1 (25)	0 (0)	0 (0)	0 (0)	0 (0)
Squamous cell carcinoma	1	1 (100)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
<b>Total</b>	<b>20</b>	<b>18 (90.0)</b>	<b>2 (10.0)</b>	<b>0 (0)</b>	<b>0 (0)</b>	<b>0 (0)</b>	<b>0 (0)</b>

**Table 4.1 Frequency of telediagnoses and recommended interventions in 955 lesions submitted for second-opinion.**

Together, the teledermatologists recommended 122 skin lesions of 112 patients to be excised or examined by a local specialist, thus resulting in a filtering percentage of 16% with regard to patients and 13% with regard to skin lesions.

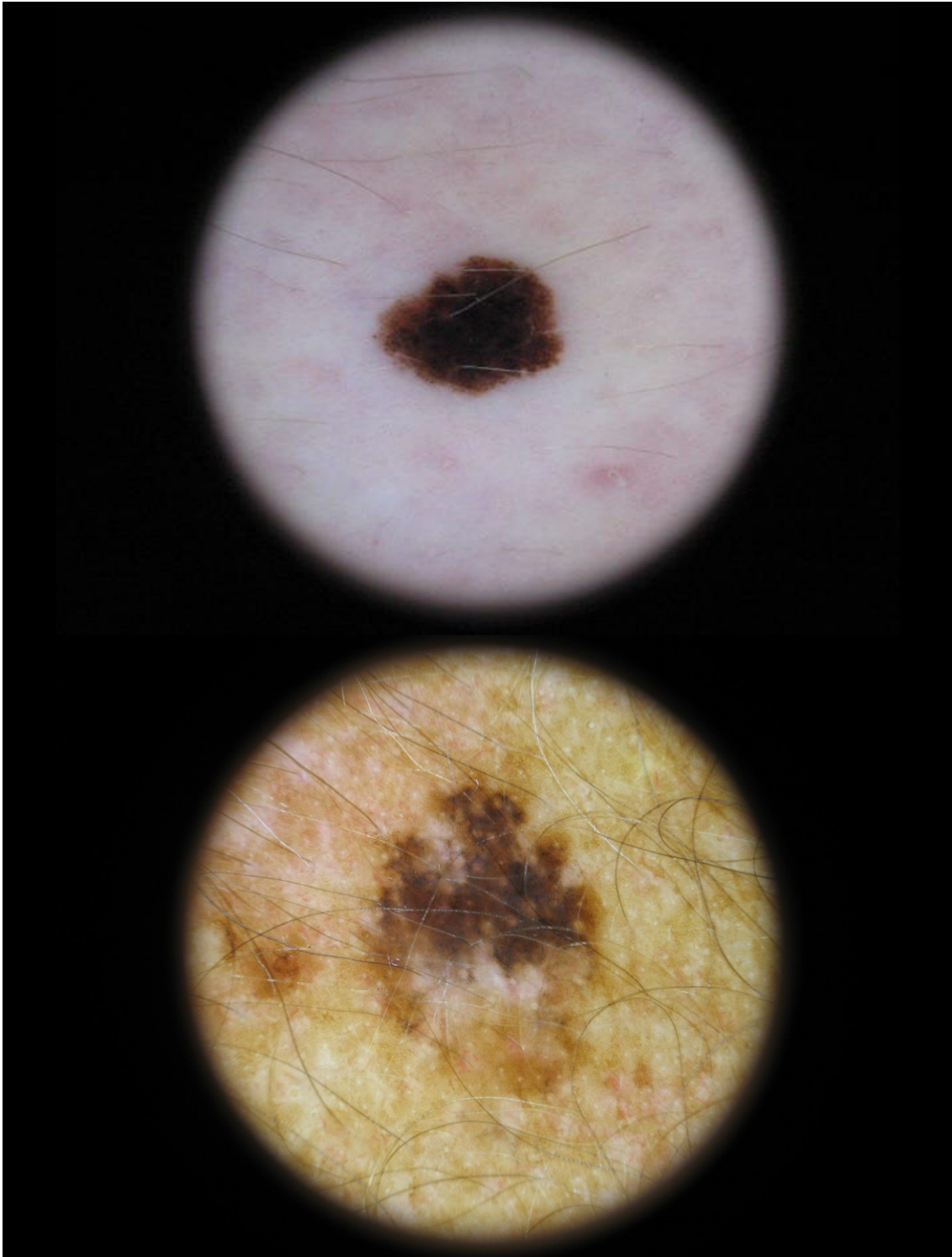
Together, 82 patients were lost to follow-up, of who 16 did not comply with the recommendation to have their lesion excised (n=13) or to be seen by a local specialist (n=3) for a further FTF examination. Thus, in only 32/122 (26.2%) skin tumours of 30/112 (26.8%) patients a “final diagnosis” (reference standard) could be established (Table 4.2): histopathology was the reference standard in 19 cases; in 13 cases, in which the specialists’ diagnoses resulted in clearly benign lesions, these FTF diagnoses were considered as the reference standard.

<b>Skin tumours</b>	<b>Reference standard (n)</b>	<b>TD Diagnosis (n)</b>
<b>Benign melanocytic</b>		
Dysplastic nevi	17	15
<b>Total</b>	<b>17</b>	<b>15</b>
<b>Malignant melanocytic</b>		
Melanoma	2	2
<b>Total</b>	<b>2</b>	<b>2</b>
<b>Benign non-melanocytic</b>		
Seborrheic keratosis	4	5
Angioma	2	2
Porokeratosis	1	1
<b>Total</b>	<b>7</b>	<b>8</b>
<b>Malignant non-melanocytic</b>		
Basal cell carcinoma	5	6
Actinic keratosis	1	1
<b>Total</b>	<b>6</b>	<b>7</b>

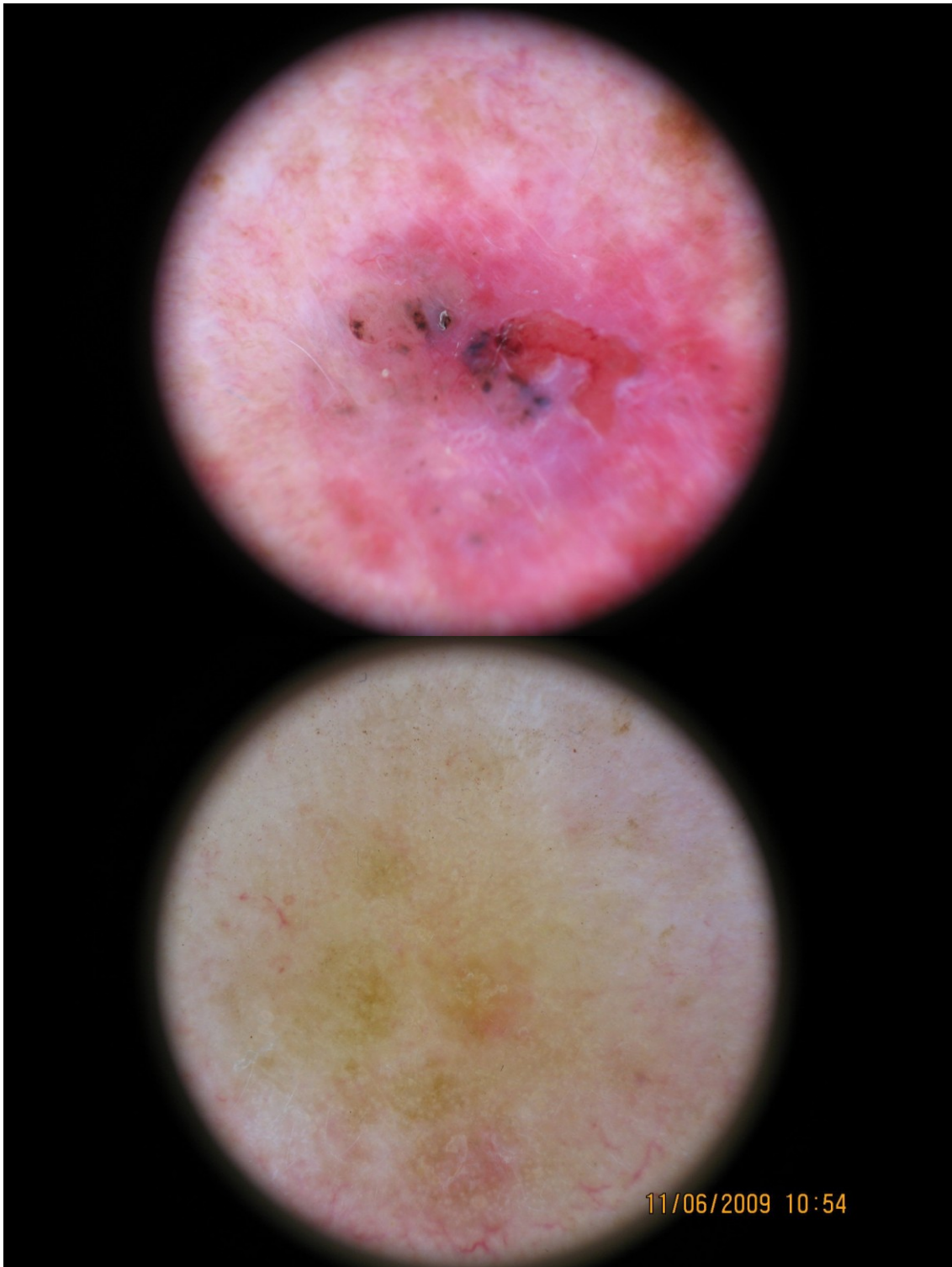
**Table 4.2 Tele dermatology diagnoses (TD) in comparison to a reference standard derived from specialist’s face-to-face results and histopathological findings**

Remote evaluations showed strong concordance with the reference standard in differentiation between benign from malignant skin lesions. Almost all lesions (n=31/32) were correctly classified by the tele dermatologists, resulting in an excellent diagnostic accuracy of 96.9%. With regard to the diagnostic accuracy for detailed diagnoses, remote diagnoses resulted in 30 (93.8%) concordant and 2

(6.2%) discordant cases. In particular, one dysplastic nevus was misclassified as a seborrheic keratosis, and another as a basal cell carcinoma. Together, all malignant (n=8) and 23/24 benign lesions were correctly disclosed by the teldermatologists (sensitivity: 100%; specificity: 95.8%). Figures 4.2 and 4.3 show several histopathologically confirmed cases of TD diagnoses.



**Figure 4.2 Dermoscopic images of a dysplastic nevus (top) and a melanoma (bottom)**



**Figure 4.3** Dermoscopic images of a basal cell carcinoma (top) and an actinic keratosis (bottom)

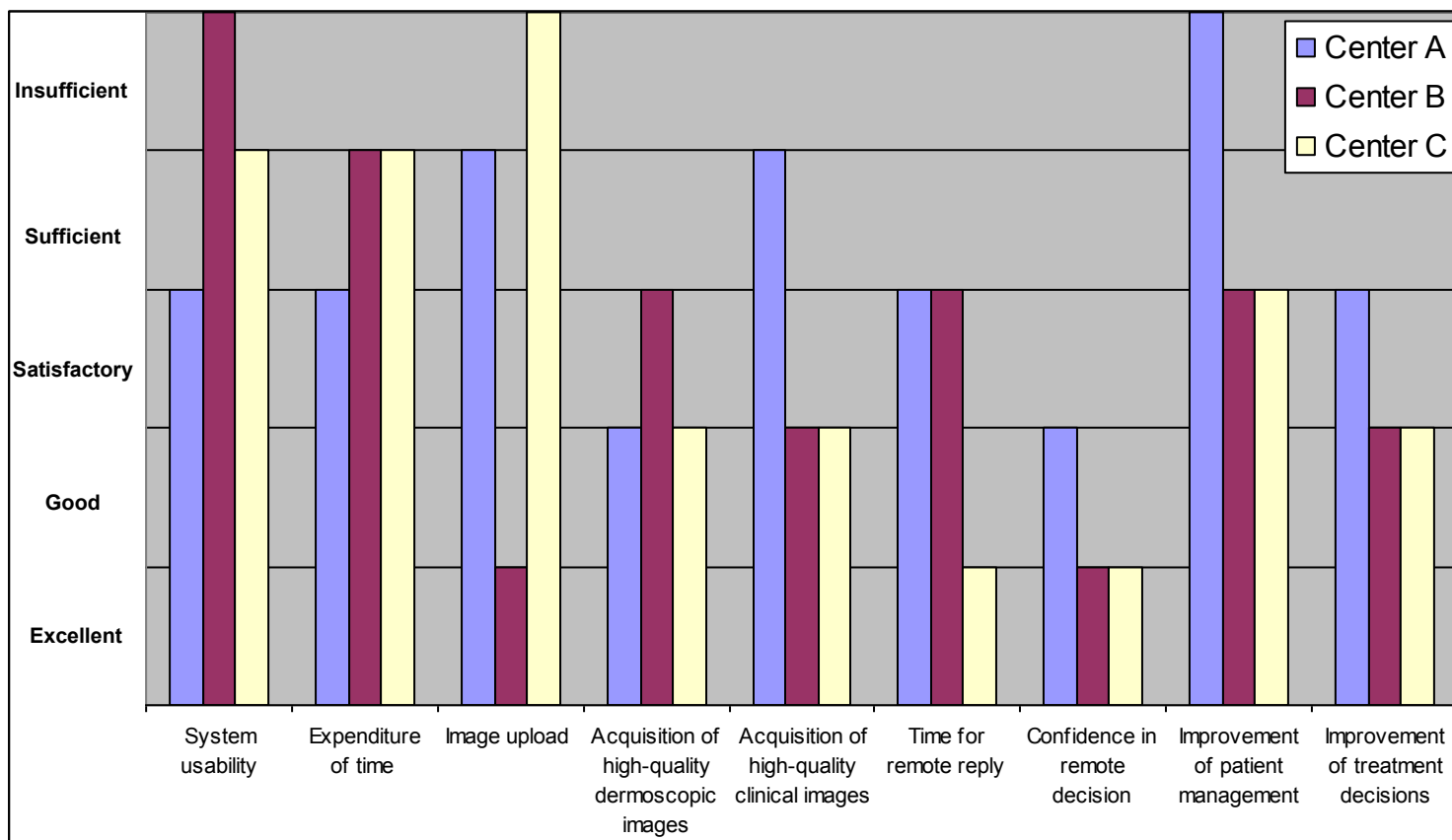
The GPs' questionnaires were returned by all seven centers. The representing GPs (n=7) of these centres, who completed the questionnaires, had a median age of 43 years, ranging from 33 to 65 years.

Four of these GPs stated not having used the system because of lacking usability of the equipment, uncertainty about the legal situation, or a general rejection of telemedicine, whereas the other 3 GPs emphasized advantages of the teleconsultation service, such as supervision and accurate decision-making. In particular, the three GPs were satisfied with the time interval for remote reply and the resulting decisions, with which they also complied in all cases. Some concerns were expressed with the increase in time required for conducting the visits compared to a conventional referral. Particularly, the complicity of obtaining constantly high quality pictures was criticized.

If no teleconsultation service had been available, the doctors stated they would have referred the patient to a specialist in cases with uncertain diagnoses.

As in their opinion the teleconsultation service rather less improved patient management, but only therapeutic decisions, they further were in disagreement among themselves about a potential usage of the teleconsultation service in their own practice.

Figure 4.4 shows GPs' ratings regarding system usability, and their acceptance of and confidence in the teleconsultation service.



**Figure 4.4 GPs' answers to questionnaire items about system usability, acceptance of and confidence in the teleconsultation service**

#### **4.4. Discussion**

A recently published extrapolation for the year 2015 acted on the assumption that there would be an increase of skin cancer by 80% (melanoma 99%, basalioma 78%, squamous cell carcinoma 80%). It was further assumed that the number of patients with skin cancer and skin cancer related problems would double in general medical practice [119].

Although the introduction of dermoscopy into the evaluation of skin growths has been shown to improve GPs' ability to triage benign versus malignant pigmented skin lesions, there are no data concerning non-pigmented skin lesions, such as squamous skin cancer.

Moreover, dermoscopy is a complex diagnostic method that demands for extensive training and a lot of experience to guarantee high diagnostic accuracy.

In this aspect, teledermatology is a reasonable tool to efficiently acquire accurate expert-opinion without the need for GPs to undergo a complex and costly training.

In the present study evaluating the applicability of a second-opinion teleconsultation service for patients attending centres for preventive health care in Austria, almost all equivocal skin tumours could be successfully teleevaluated (99.7%), and a definitive management decision could be established in all of these cases.

A recommendation to follow-up lesions was given in 73.8% of the cases, particularly for atypical nevi, resulting in a slightly higher follow-up rate compared to previous studies [116].

Our results, however, seem to be comparable to those of routine practice, for which a follow-up of nevi in a 3-, 6-, or 12-month interval is generally recommended, depending on the potential of malignant exacerbation of a given lesion [120, 121, 122].

In 13% of the cases, malignancy was suspected, why an excision or a referral to a local specialist for a further FTF examination was recommended.

After excluding the cases lost to follow-up, the diagnostic accuracy for these cases was excellent and comparable to that of previous studies [10, 106, 107, 108, 109]

In contrast to those, however, in our analysis, only primary diagnoses were taken into account, thus a concordance rate of 93.8% (n=30/32) for detailed diagnoses and a concordance rate of 96.9% for tumour categories was quite excellent. Moreover, all (n=8) malignant lesions had been correctly diagnosed by the teledermatologists resulting in a sensitivity of 100%.

Regarding specificity, only two dysplastic nevi were misdiagnosed as either a seborrheic keratosis or a basal cell carcinoma.

This might have been due to the fact that precise dermoscopic guidelines for the diagnosis of non-melanocytic skin lesions are still missing yet [78]. However, also imprecise clinical data, missing clinical images, or a low image quality itself, might have impeded the establishment of a correct remote diagnosis in these cases.

A main limitation of the present study was the small number of skin lesions that could be included in the analysis, as many patients were lost to follow-up (n=82). A further limitation include the missing histopathologic diagnosis in a large amount of skin lesions with suspected malignancy, which otherwise might have served as a fertile reference standard to which to assess diagnostic accuracy.

In contrast to recent studies [21, 98, 123], in which doctors were pleased with the teleconsultation system, in the present study, GPs' acceptance of and confidence in the teleconsultation service was rather low.

Reasons for that were may be assumed as follows: firstly, telemedicine is not commonly used in Austria, secondly, legal guidelines and wages for telerequesting doctors are still missing, thirdly, the request process is quite time-consuming. The GPs, however, also emphasised advantages of the teleconsultation service. In particular, they were satisfied with the quality of remote decisions and they stated that the second-opinion somewhat facilitated their treatment decisions. Nevertheless, as in their opinion, the teleconsultation service rather less improved patient management, they were in disagreement among themselves about a potential future usage of the teleconsultation service, particular in their own practice.

## **4.5. Conclusion**

In view of the fact of continuously increasing incidence rates of skin cancer, prevention is becoming a crucial topic in our medical system.

Second-opinion teleconsulting may have the ability to triage out clearly benign lesions, allowing obvious malignancy and equivocal lesions to be appropriately managed by non-experts such as GPs.

Thus, TD may offer a cost-effective possibility to extend skin cancer screening to the broad public and improving secondary prevention by detecting more lesions in a pre-malignant- or early stage of the disease.

Patients may widely accept second-opinion teledermatology services in this context, and also comply with remote treatment/management decisions in most of the cases. Physicians, however, seem to be quite less satisfied with such services, particularly due to unimproved complicated, and time-consuming workflows, which, further are not financially compensated yet. Moreover, missing legal guidelines for telemedicine services may induce reservations against teledermatology applications in general.

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