In vivo reflectance confocal microscopy, a novel non-invasive tool for diagnosing skin cancer - a randomized controlled trial

Published: 30-11-2015
Last updated: 19-04-2024

RESEARCH QUESTION(S): Can in vivo reflectance confocal microscopy (RCM) correctly identify the subtype of basal cellcarcinoma (BCC)?Primary Objective: To study whether in vivo reflectance confocal microscopy (RCM) can correctly identify the subtype…

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Skin neoplasms malignant and unspecified
Study type	Interventional

Summary

ID

NL-OMON42736

Source
ToetsingOnline

Brief title
RCM in basal cell carcinoma

Condition

- Skin neoplasms malignant and unspecified

Synonym
basal cell carcinoma, skin cancer

Research involving
Human

Sponsors and support

Primary sponsor: Radboud Universitair Medisch Centrum

Source(s) of monetary or material Support: ZonMw,Mavig: Wij krijgen voor de loop van het onderzoek een extra RCM apparaat ter beschikking gesteld

Intervention

Keyword: basal cell carcinoma, cost-effectiveness, diagnosis, Reflectance confocal microscopy

Outcome measures

Primary outcome

Primary Objective: To study whether in vivo reflectance confocal microscopy

(RCM) can correctly identify the subtype of BCC.

Primary outcome measure is defined as:

- Correct sub-typing of BCC after excision.

Secondary outcome

Secondary outcome measures:

- QoL

- Cost

- QALY's

- The ability of RCM to separate sBCC from other BCCs

- Development of guidelines and protocols for future RCM users.

Study description

Background summary

Skin cancer (SC) is the most common cancer and its incidence is increasing rapidly in Western countries.(8-9) In the Netherlands the registry of SC is poor, however based on recent literature and guidelines we estimate the number of new malignant skin tumours and the precursor actinic keratosis (AK) in 2015

at around 235,278, having a major impact on our health care system. Moreover, it is predicted that numbers of SC will rise with 4.5-8% per year, depending on the type of skin cancer. SC comprises melanoma (MM) and non-melanoma SC (NMSC: basal cell carcinoma (BCC), squamous cell carcinoma (SCC) and its precursors actinic keratosis (AK) and Bowen disease). In case of suspicion on NMSC, at present, the pathological examination of a biopsy is the gold standard. In the US, already in 2003, SC was found to be among the most costly of all cancers to treat, thus, it is evident that SC places an enormous burden on western healthcare systems with increasing costs.(1) As BCC is the most common SC with an estimated incidence of 51,000 new tumours in 2015, with the conventional diagnostic procedure we experience in 29% of the cases a sample error, so the subtype is not correct. Treatment choices depend on BCC subtype, thus the correct sub-typing is very important.

HEALTH CARE EFFICIENCY PROBLEM and RELEVANCE FOR PRACTICE

As described above, the incidences of the various malignant skin tumours are increasing dramatically. The rising number of SC may result in long waiting lists for consultation at departments for dermatological care and in increasing health care costs. In case of suspicion on SC it is of utmost importance to diagnose and treat in an early phase, preferable in a patient friendly manner. SC is responsible for 50% of the costs in dermatological patient care, 75-80% of these costs are caused by BCC. These costs will increase even more, as incidence rates will rise further. As described above, the gold standard is pathological investigation of a biopsy or of an excision. However, pathological diagnosis of a biopsy often results in sampling errors, as only a small part of the tumour is investigated resulting in potentially inappropriate chosen therapies. The subtypes of BCC are treated differently. As a sample error may lead to treatment failures or recurrences, other subsequent treatments are needed, increasing costs. In addition, the conventional method is unfriendly for patients, as it is invasive, painful, scarring, and the diagnosis is not instantly available. In order to implement patient friendly RCM in daily BCC care, a large prospective study is needed. The ability of RCM in determining the correct diagnosis and sub-typing needs to be investigated as well as preparing protocols for use in patient care. With implementation of RCM we aim to contribute to these demands as we believe that this diagnostic imaging technique will be more cost-effective and more patient friendly as compared to the biopsy procedure, the gold standard at present. We intend, in case our future studies demonstrate the expected advantages of RCM, to advise to adjust guidelines with respect to our past and future results.

With the implementation of RCM in routine patient care settings the diagnosis is assessed at the first consultation and the patient can be treated instantly. A second consultation for explaining the diagnosis is than not necessary, which time can then be used for other new patients. Also, with the conventional diagnostic procedure (pathological investigation of a skin biopsy) we experience in 29% of the cases a sample error (10), so the BCC subtype is not correctly identified, and as treatment depends on BCC subtype many patients need a subsequent treatment because of treatment failure or recurrence. Also for pathologists, to examine skin tumour after skin tumour is not that

efficient and challenging. More pathologists are needed if we don*t try to search for other diagnostic techniques. RCM will also, not unimportantly, lower the costs for diagnosing SC. Currently, in case of suspicion on NMSC, including BCC, an invasive diagnostic biopsy for pathological examination is performed. (Guidelines NVDV)
At present, the use of RCM imaging for diagnosing SC in clinical practice is increasing in Italy and Germany. However, in the Netherlands, the use of this technique is only limited to research. This is mainly caused by the differences in insurance and healthcare systems between these countries. A large scale prospective study on assessment of the BCC subtype, which is lacking in international literature, is needed to implement this diagnostic technique in the Dutch healthcare system. Implementation of RCM imaging in our health care system may result in patient friendly and instant diagnosis, cost reduction, reduction of sampling errors, reduction of inappropriate treatment choices and unnecessary diagnostic excisions.
Besides the patient friendliness, implementation of RCM in patient care is important from an economic point of view. Costs for pathologist, manpower, materials, appointments, inappropriate therapies, leading to subsequent therapies because of treatment failures decrease. Yearly avoidable costs are estimated for our center at ¤ 225,179. About ¤141 per BCC avoided can be saved. Investment in RCM is about ¤250.000 and will be depreciated over 10 years. Yearly variable cost for RCM are ¤54,000. This means reasoning from the Radboudumc 2014 production that costs per RCM diagnosis are ¤49. From this we infer that net savings are ¤92 per biopsy avoided (¤147.200 yearly for our center) and even more if economies of scale are exploited nationally (¤ 4692000). If in future 40-50% of all SC can be imaged by RCM, meaning on a national basis 94000 tumours, total yearly national savings will then be around ¤ 8648000 (conservative estimate).

Study objective

RESEARCH QUESTION(S): Can in vivo reflectance confocal microscopy (RCM) correctly identify the subtype of basal cell
carcinoma (BCC)?

Primary Objective: To study whether in vivo reflectance confocal microscopy (RCM) can correctly identify the subtype of BCC.

Primary outcome measure is defined as:
- Correct sub-typing of BCC after excision.

Secondary outcome measures:
- QoL
- Cost
- QALY's
- The ability of RCM to separate sBCC from other BCCs

- Development of guidelines and protocols for future RCM users.

Study design

Randomized controlled trial. In this design it is possible to obtain empirical estimates of the (cost-)effectiveness in daily clinical practice, beyond the diagnostic value. Patients with lesions clinically suspicious for BCC, eligible for RCM, visiting the dermatological departments of the Radboud University Medical Center, Nijmegen, the Canisius Wilhelmina Hospital Nijmegen, and the Rijnstate Hospital Arnhem-Velp, The Netherlands, will be asked to participate in this study in the period December 2015-December 2018. During the last 12 months we will finalize our database with all data and images and perform the analyses.
The follow up period is three months.

PATIENT OUTCOME ANALYSIS The effect analysis adheres to the design of a randomized controlled trial and measures diagnostic performance and quality of life at baseline, and at fixed points along the follow-up of the clinical trial (see design clinical trial). To measure the quality of the health status of the patients a validated so-called health-related quality of life (HRQoL) instrument will be used, the EuroQol-5D (EQ-5D) (Dolan, 1997). This HRQoL instrument will be completed by the patients and is available in a validated Dutch translation (Lamers et al., 2005). The EQ-5D is a generic HRQoL instrument comprising five domains: mobility, self-care, usual activities, pain/discomfort and anxiety/depression. The EQ-5D index is obtained by applying predetermined weights to the five domains. This index gives a societal-based global quantification of the patient*s health status on a scale ranging from 0 (death) to 1 (perfect health). Patients will also be asked to rate their overall HRQoL on a visual analogue scale (EQ- 5D VAS) consisting of a vertical line ranging from 0 (worst imaginable health status) to 100 (best imaginable). The patient outcome analysis will be complemented with a CVM questionnaire and measures of satisfaction and pain related to diagnosing subtype BCC.

Intervention

In one group, 3 mm skin biopsies will be performed, this is the conventionale regular diagnostic method which is invasive.
In the other group, in vivo reflectance microscopy will be performed, this is the novel daignostic method, which is non-invasive.

Study burden and risks

The RCM-imaging itself is non-invasive, safe and painless. The 3mm punch biopsy of the skin tumour is limited invasive, but is at present common practice in case of suspicion on BCC. We would also perform a diagnostic biopsy if the patient would not be included in this study. Risks of the biopsy procedure are

generally small, consisting of continued bleeding and infection. These are generally localised and can be treated easily. In future taking biopsies may be replaced by RCM-imaging. This could be useful for the patient himself and for others. Skin could then be evaluated painlessly and non-invasively. Also filling in the questionnaires may ask some time. The duration of this visit will approximately take one hour. Treatment of a pathological proven BCC is also normal practice, surgical excision is appropriate in these cases. Minors and incapacitated subjects will not be included.

Contacts

Public
Radboud Universitair Medisch Centrum

Rene Descartesdreef 1
Nijmegen 6525 GL
NL
Scientific
Radboud Universitair Medisch Centrum

Rene Descartesdreef 1
Nijmegen 6525 GL
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

- Age *18 years
- Patient must be able to adhere to all requirements of the study

- Patient must be willing to give written informed consent
- Clinically diagnosed/ clinical suspicion of basal cell carcinoma

Exclusion criteria

- Participating in other investigational research currently or in the previous 28 days before the study
- Patient is having a medical condition which excludes participating the research, according to the investigator
- Incapacitated subjects will not be included
- Lesion(s) on parts of the body which do not allow to adequately image the tumour with RCM.

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Diagnostic

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	24-02-2016
Enrollment:	329
Type:	Actual

Ethics review

Approved WMO

Date:	30-11-2015

Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	08-01-2016
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	25-01-2017
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
CCMO	NL54549.091.15