# Clinical diagnosis versus histological diagnosis by punch biopsy to determine the subtype of basal cell carcinoma

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To establish the diagnostic value of clinical diagnosis to predict the histological BCC subtype and compare this by the diagnostic accuracy of PB to determine the subtype of BCC in the subsequent SE/MMS specimen.

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| **Ethical review** | Approved WMO |
| **Status** | Recruiting |
| **Health condition type** | Skin neoplasms malignant and unspecified |
| **Study type** | Observational invasive |

## Summary

### ID

NL-OMON36694

**Source**
ToetsingOnline

**Brief title**
Clinical diagnosis of basal cell carcinoma subtype

### Condition

- Skin neoplasms malignant and unspecified

**Synonym**
Basal cell carcinoma, skin cancer

**Research involving**
Human

### Sponsors and support

**Primary sponsor:** Medisch Universitair Ziekenhuis Maastricht
**Source(s) of monetary or material Support:** Ministerie van OC&W

## Intervention

**Keyword:** Basal cell carcinoma, Biopsy, Clinical, Diagnosis

## Outcome measures

### Primary outcome

Of both the clinical diagnosis and the punch biopsy:

- Sensitivity

- Specificity

- Positive predictive value

- Negative predictive value

### Secondary outcome

To assess the inter-observer and intra-observer variability of dermatologists

and pathologists to determine subtype BCC.

# Study description

### Background summary

Basal cell carcinoma throughout the world
Skin cancer is the most common form of cancer, with basal cell carcinoma (BCC) being the most frequent form of all skin cancers, and the incidence is still rising without future signs of a plateau. Because there is no national registry for BCC in the Netherlands, incidence rates are derived from the only register centre in the southern part of our country. From a recent study we know that approximately 26.625 new patients with BCCs occurred in 2006 in the Netherlands. The average number of BCC per patient is 1.65, resulting in 44.000 new BCCs in that year. With an increase of approximately 10% per year the estimated incidence rate at 2011 will be around 70.800 in the Netherlands.
Three important histopathologic subtypes of BCC can be distinguished, namely superficial, nodular and aggressive. In the past, nodular basal cell carcinoma (nBCC) was the most common histopathologic subtype, but superficial basal cell carcinoma (sBCC) and aggressive basal cell carcinoma (aBCC) are the subtypes with the fastest growing incidences. Nowadays, the distribution of histopathologic subtypes of BCC is 40.6% nodular, 30.7% superficial and 28.7%

aggressive. The shift from nodular BCCs to other subtypes needs accurate detection of the correct subtype, as treatment per subtype is different. The sharp raising incidence of 10% annually makes BCC an even bigger health problem in the near future.

Diagnosis of BCC
BCC is diagnosed with a 3 mm punch biopsy (PB) of the suspected skin lesion. Based on the most aggressive histopathologic subtype seen in this biopsy, an appropriate treatment is chosen. Three subtypes are relevant for a suitable treatment choice: superficial, nodular and aggressive. The last one includes all BCCs with aggressive growth, such as infiltrative/morpheaform BCC, micronodular BCC, and BCC with squamous differentiation. Unfortunately, 31-33% of histopathologic subtypes seen on punch biopsies of primary and recurrent BCCs do not correspond with the subtype seen in the subsequent surgical excision (SE)/ Mohs micrographic surgery (MMS). The consequence is overtreatment and undertreatment.

Guidelines on the treatment of basal cell carcinoma
The national advisory board of Dutch dermatologists and plastic surgeons has published multidisciplinary guidelines on the treatment of BCCs in 2007. In these guidelines the different treatment options for all sort of BCCs are discussed and conclusions are drawn for each treatment option. Recommended treatments for all BCCs regardless of the histopathological subtype is SE. Both sBCC and nBCC have to be excised with 3 mm margin while aggressive subtypes need a 5 mm margin. BCCs in the H-zone will be excised with MMS. Photodynamic therapy (PDT), Imiquimod and 5-fluorouracil (5-FU) are also options for sBCC on low-risk sites because of better cosmetic results.Recent studies show overall estimated treatment success at 5-year follow-up of 65% for PDT and 78-80% for Imiquimod. These percentages are far lower than the 99% overall estimated treatment success of SE in sBCC. There is no literature on treatment effect of 5-FU at long term follow-up. Only two studies report 86-87% complete response rate to different 5-FU treatment regimens after 6-12 weeks.

Treatment of basal cell carcinoma at the Maastricht University Medical Center (MUMC) and Erasmus Medical Center (Erasmus MC) Rotterdam.
In the past, BCC has been a disease of the elderly patient but as a consequence of recreational sun exposure and tanning beds, more young patients develop a skin cancer as well. Therefore, cosmetic results play a more important role when choosing a suitable treatment. Therefore in today*s dermatologic practice at the MUMC and Erasmus MC patients with a sBCC can be treated non-invasively with PDT, Imiquimod, 5-FU or with SE/MMS. These non-invasive treatments show good cosmetic results but higher recurrence rates than SE. Any non-responding or recurrent sBCC has to be retreated with SE/MMS.

Undertreatment and overtreatment
Preliminary data from our own study show that in case of a discrepancy between histopathologic BCC subtype in the PB and excision, 58% of patients are

overtreated and 42% undertreated. Half of the overtreated patients will have a histological nBCC or aBCC on PB, but only superficial in the SE/MMS. This could be partly due to the fact that the most suspected part has already been biopsied and is not present in surgical excision anymore.
Overtreatment consists of unnecessary tissue loss because of too wide SE margins. In addition, large excisions might lead to more complications like scarring, infection, continued or subsequent bleeding and dehiscent wounds. Undertreated patients have to be re-treated again in case of positive resection margins with SE, resulting in extra stress for patients, time and health care costs.

Clinical diagnosis
Histological diagnosis of BCC subtype by PB might not be the perfect procedure because of the 30% mismatch with the subtype seen in the SE/MMS. A potential better way to determine the BCC subtype might be the clinical diagnosis. To our knowledge, there is no literature about the sensitivity and specificity of the clinical diagnosis to determine the subtype of BCC seen in the SE/MMS specimen. We want to confirm the hypothesis that the clinical diagnosis is as good as or even better than the histological diagnosis by PB to determine the BCC subtype compared to the gold standard of SE/MMS. Confirmation of this hypothesis will result in clinical diagnosis instead of punch biopsies, more patients receiving early and correct treatment, saving time and health care costs. The conclusions from the proposed study can serve as a basis for updating guidelines for the diagnosis of BCC.

## Study objective

To establish the diagnostic value of clinical diagnosis to predict the histological BCC subtype and compare this by the diagnostic accuracy of PB to determine the subtype of BCC in the subsequent SE/MMS specimen.

## Study design

Clinical, prospective, multi-centre study

## Study burden and risks

There is no burden for patients with nBCC or aBCC. The will be treated according to regular care.

The burden for patients with a sBCC is minimal. The visits and procedures that will take place mostly don't differ from regular care like physical examination, photography and punch biopsy. In regular care, patients can choose between surgical treatment with low recurrence rates or non-invasive treatment with better cosmetic results. Patient who participate in the study have no choice and will all be treated with SE or MMS.

The SE will approximately take 30 minutes and the MMS 2-8 hours, depending on the number of excisionrounds. After injection with a local anaesthetic this is a painless procedure. The injection can give a burning sensation. Risks of surgical excision might be scarring, continued or subsequent bleeding, infection or dehiscent wounds.

# Contacts

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# Trial sites

## Listed location countries

Netherlands

# Eligibility criteria

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

## Inclusion criteria

Minimal age of 18 years
Maximum of 3 clinical suspected BCCs
Primary BCCs (no previous treatment)
Being able to understand instructions

### Exclusion criteria

Age under 18 years
More than 3 clinical suspected BCCs
Recurrent BCCs (previously treated)
Not able to understand instructions
Concomitant disease requiring systematic immunosuppressive treatment
Genetic skin cancer disorders

## Study design

### Design

**Study type:** Observational invasive

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| Masking: | Open (masking not used) |
| Control: | Uncontrolled |
| Primary purpose: | Diagnostic |

### Recruitment

NL

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| Recruitment status: | Recruiting |
| Start date (anticipated): | 16-08-2011 |
| Enrollment: | 158 |
| Type: | Actual |

## Ethics review

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| Approved WMO Date: | 11-08-2011 |
| Application type: | First submission |
| Review commission: | METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht) |
| Approved WMO Date: | 13-02-2012 |
| Application type: | Amendment |
| Review commission: | MEC academisch ziekenhuis Maastricht/Universiteit |

# 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 |
|---|---|
| ClinicalTrials.gov | NCT01370824 |
| CCMO | NL35344.068.11 |