

## **Infrared thermography**

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REVIEW ARTICLE

## Infrared thermography: a scoping review of its possible role in the diagnosis and follow-up of leprosy neuropathy

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**Summary** Neuropathy is a well-known complication of leprosy. Nerve palpation and assessment of motor and sensory nerves are routinely performed at diagnosis in leprosy, which helps establish the diagnosis and, during treatment, monitor the status of somatic nerve function. Assessment of peripheral autonomic nerve function is not commonly practiced for diagnosing leprosy or for diagnosing and monitoring neuropathy. Early impairments in autonomic function, however, may help to establish or confirm a diagnosis and predict the development of clinical leprosy and neuropathy. Several studies, including infrared thermography and electro-neurophysiological studies, have shown the presence of subclinical nerve impairments that may indicate a diagnosis of leprosy or lead to the development of neuropathy. Sudomotor and vasomotor impairments, in the presence of loss of protective sensation, also increase the risk for ulceration, often requiring chronic care. This article provides a brief discussion of the importance and assessment of peripheral autonomic nerve function in leprosy. Its focus is to review articles that have used infrared thermography to assess this function.

**Keywords:** Leprosy, Hansen's disease, neuropathy, assessment, infrared thermography, autonomic nerve function

### Introduction

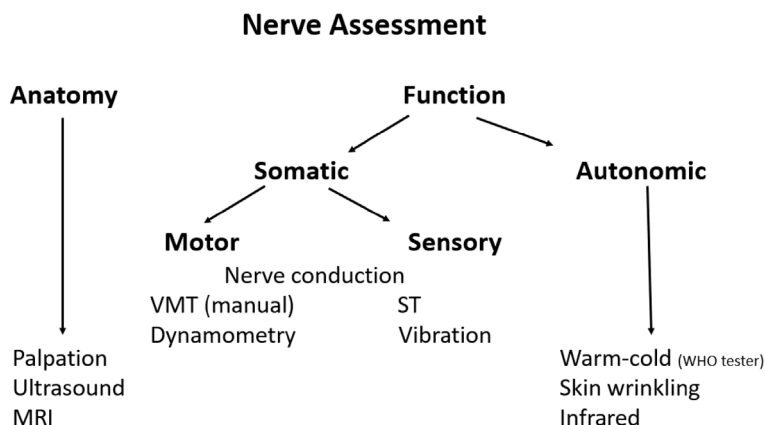
Leprosy is an infectious disease with low pathogenicity, primarily affecting the skin and superficial peripheral nerves. Approximately 180,000 patients are diagnosed with this condition annually, primarily in low-resource countries.<sup>1–4</sup>

The diagnosis of leprosy is typically made in the presence of one or more of the three so-called cardinal signs: a positive skin smear for *Mycobacterium leprae*, hypopigmented skin lesions accompanied by loss of light touch, and one or more enlarged peripheral nerves.<sup>4,5</sup>

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Patients without typical leprosy skin lesions may be diagnosed with “neural” leprosy, and skin smears are negative.<sup>6–8</sup>

Routine nerve function examinations used to establish a diagnosis are limited to somatic nerve function, including voluntary muscle testing (VMT) and sensory testing (ST).<sup>9,10</sup> The assessment of autonomic nerve function is hardly practiced (see Figure 1). Although some techniques have been developed, none have been routinely adopted.<sup>11–14</sup>



**Figure 1.** Nerve function assessment in neuropathies and nerve lesions. VMT: Voluntary muscle testing; ST = Sensory testing; Magnetic Resonance Imaging. WHO tester.<sup>12</sup> Autonomic: a distinction could be made between sudomotor and vasomotor function.

Some studies have used the inspiratory gasp to elicit a peripheral autonomic response, sometimes in conjunction with cold stress testing.<sup>15–19</sup> Again, these tests are not widely employed in everyday practice.

Many studies have suggested that subclinical impairment in nerve function can be one of the first indicators of leprosy or leprosy neuropathy, as evidenced by delayed sensory nerve conduction and vasomotor reflex testing.<sup>13,15–17,20–22</sup>

The consequences of loss of peripheral autonomic nerve function can be significant: loss of sweating resulting in skin dryness, a major predisposing cause of ulceration when superimposed on sensory loss, as it usually is.

In general practice, comparing two contralateral sites, feeling a raised skin temperature points to inflammation. Measuring skin temperature with a thermometer can quantify this, but infrared thermography can do this more accurately and visualize temperature changes. Raised skin temperatures or differences in skin temperature between similar body parts could play a crucial role in the early diagnosis of leprosy neuropathy, confirming or supplementing the diagnosis. This article focuses on studies that discuss the assessment of the Autonomic Nervous System (ANS) function and explores the potential applications of Infrared Thermography (IRT) in the diagnosis and management of leprosy and leprosy neuropathy.

Research on the use of IRT in leprosy needs to address some of the following questions:

To what extent does autonomic nerve impairment (ANI) occur independently of somatic nerve function loss as a possible early indicator for developing clinical leprosy or (subclinical) neuropathy? Can IRT confirm or supplement the early diagnosis of leprosy? What are the

potential differences in the presence and extent of Autonomic Nerve Impairment (ANI) in the leprosy classification spectrum?

These and other questions will not be answered in this overview of possible use. IRT will be presented as a relatively new assessment technique that could benefit the diagnosis and management of leprosy neuropathy and its consequences.

## **Method**

The two main keywords used in the search for relevant articles are “leprosy” and “thermography.” Article references were reviewed for potential additional documents pertinent to the assessment of leprosy autonomic dysfunction.

Infolep, (INFOrmation LEP) is a database developed explicitly for leprosy.<sup>23</sup> Searching this database with “thermography” yielded 20 articles, of which 12 were considered essential to extract information relevant to the diagnosis and possible follow-up of leprosy neuropathy.

The PubMed search yielded 18 articles with the same keywords. We read and checked the references for these articles to identify possible additional sources.

Google Scholar was hand-searched with an extended string adding the word “neuritis/neuropathy” (neur\*), N 77. These articles were hand-searched, and reference checking was conducted for all relevant publications, particularly “review” articles, assuming that important articles that could be verified would be listed.

Finally, Science Direct showed 81 articles with the “Thermography AND Leprosy” string.

Due to the many similarities between diabetic and leprosy neuropathy, as well as their consequences, articles related to diabetes have been included in this paper when deemed relevant to illustrate the use of thermography in the diagnosis, assessment, and follow-up of nerve function impairment.

No attempt was made to conduct a comprehensive review of the use of thermography in diabetes or other diseases, nor was there an attempt to qualitatively grade the reviewed articles.

## **Infrared thermography in leprosy**

IRT is a well-established imaging technique in general medicine and can be considered a proxy assessment for autonomic nerve function.<sup>24,25</sup> The indications for using infrared thermography in leprosy can be considered in two distinct groups. Applications related to the diagnosis and follow-up of the disease, including neuropathy, and indications that relate to the consequences of impaired neural function.

### **DIAGNOSIS OR CONFIRMATION OF THE DISEASE**

The presence of one or more of the three cardinal signs determines the diagnosis.<sup>4</sup> Without clear cardinal signs, the findings of IRT research can increase the likelihood of a diagnosis, confirm it, and enhance the accuracy of the diagnosis.<sup>26,27</sup> Illarramendi reported a high prevalence of vasomotor reflex impairment in newly diagnosed patients with laser Doppler velocimetry.<sup>18</sup>

### **NERVES-NEUROPATHY**

Balbinot (2012) and Zhou (2021) used thermography to diagnose early diabetic neuropathy.<sup>28,29</sup> Neuropathy is a critical component of leprosy, which is usually considered a dermatological disease. Neuropathy/neuritis may lead to loss of sensation and paralysis, often leading to well-known secondary, frequently preventable impairments and deformities.<sup>30</sup>

Monitoring leprosy neuropathy is crucial for assessing the effectiveness of treatment and taking prompt action when new nerve impairment is detected. Treatment results depend on factors such as age, classification, treatment efficacy, and duration of nerve function loss. IRT could be a functional adjunctive assessment in following neuropathy and its possible progression or resolution. No studies have been found that use IRT in follow-up assessments of nerve function impairment, either in its natural course or following medical or surgical interventions such as neurolysis.

#### SKIN LESIONS

Skin lesions are a typical cardinal sign of leprosy. They are usually described as anesthetic or insensitive; “hypo-aesthetic” is a better term. Is skin temperature impaired, maybe compared to the contralateral side? Does reduced touch sensation parallel *a reduction or an increase in temperature* when patients have leprosy reactions? Could IRT again be a valuable tool in monitoring and evaluating temperature recovery following treatment?<sup>31,32</sup> Rodrigues, using a thermal sensory analyzer—not infrared—showed temperature differences between skin lesions and the symmetrical contralateral skin.<sup>33</sup> Srinivasan and Stumpe developed a simple hand-held battery-operated pen-like instrument to detect temperature differences between normal and affected skin.<sup>34</sup>

#### NEUROPATHIC PAIN

Tiago *et al.* used IRT to assess neuropathic pain (2021). They concluded, “IRT confirmed the asymmetric pattern of leprosy neuropathy, indicating a change in the function of the autonomic nervous system, and proved to be a useful method in the approach of pain.”<sup>35</sup>

#### ULCERATION AND “HOT” FEET

“The foot heats up before it breaks down”<sup>36</sup> (Paul Brand in Boulton)

The leading secondary, preventable complication following leprosy neuropathy is ulceration, especially plantar ulceration. In a well-functioning program, individuals with loss of protective sensation should be educated on how to care for their feet and be aware of signs such as swelling and *elevated temperature*.<sup>35–37</sup>

Boulton pointed out the many similarities between leprosy and diabetes-related neuropathy in plantar ulceration. Several studies have been conducted on diabetic neuropathy to evaluate skin temperature as a risk factor for plantar ulceration and to monitor its healing process.<sup>36</sup>

Armstrong *et al.* conducted a physician-blinded study comparing two groups of patients with neuropathic feet. Both received standard care. The experimental group monitored their feet with a skin thermometer. High temperature gradients between feet may predict the onset of neuropathic ulceration, and self-monitoring may reduce the risk of ulceration.<sup>38</sup> Of course, in diabetes, besides impaired vasomotor reflexes, impaired function is compromised by vascular pathology.<sup>39–41</sup>

#### CONTACT EXAMINATION

Studies indicate that social, environmental, and genetic factors may contribute to the development of leprosy.<sup>42,43</sup> As stated, multiple electro-neurophysiological studies also confirm that either subclinical somatic or autonomic nerve function impairments may be present in the contacts of leprosy-affected people.<sup>44–46</sup>

Using infrared thermography, Sabino and dos Santos showed changes in asymptomatic household contacts and concluded that IR thermography may detect temperature asymmetry in the hands of leprosy contacts, indicating peripheral autonomic dysfunction related to early neural impairment in these individuals.<sup>45–48</sup>

## Discussion

This article emphasizes the importance of early diagnosis of leprosy neuropathy and the potential role of thermography in the diagnostic process (Table 1). This includes not only neuropathy but also possible assessment and follow-up of the consequences of nerve function impairment. Notably, thermography is not mentioned in two leading textbooks on leprosy.<sup>49,50</sup> It is essential to know that in leprosy, autonomic impairments are usually present when sensory and motor impairments are present. However, autonomic innervation can be unaffected with impaired sensation or motor function in other neurological diseases and can, therefore, be important in the differential diagnosis.<sup>51</sup>

**Table 1.** Selected quotes illustrating the importance of assessment of Autonomic Nerve Function (ANF) in the early diagnosis of leprosy neuropathy

| Quote                                                                                                                                                                                      | Authors                                | Year |
|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------|------|
| <i>“...the detection of impaired VMRT distinguished newly registered leprosy patients from healthy controls”</i>                                                                           | Abbot, Swanson Beck <sup>15</sup>      | 1991 |
| <i>“Subclinical autonomic neuropathy is common among healthy contacts of leprosy patients....”</i>                                                                                         | Wilder-Smith <sup>40</sup>             | 1997 |
| <i>“A high prevalence of peripheral autonomic dysfunction...was observed in newly diagnosed leprosy patients.....autonomic nerve lesion was more frequent than somatic lesions...”</i>     | Illarramendi <sup>18</sup>             | 2005 |
| <i>“Basic research (nerve conduction) has shown that nerve impairment is detectable long before it turns clinical”</i>                                                                     | Wilder Smith, van Brakel <sup>65</sup> | 2008 |
| <i>“Thermography proved a potential tool... to assist in the early detection of neuropathies...” ...a significant interaction between clinical form of leprosy and the temperature...”</i> | Cavalheiro <sup>19</sup>               | 2016 |
| <i>“Temperature diminished in leprosy patients compared to healthy controls” – “detect asymmetry to detect early autonomic dysfunction”</i>                                                | Sabino, Dos Santos. <sup>47</sup>      | 2023 |
| <i>“Detecting asymmetry in hands of leprosy contacts”</i>                                                                                                                                  | Sabino, Dos Santos. <sup>46</sup>      | 2024 |

VMRT – Vaso motor reflex testing.

Table 2 lists recent studies using thermography in leprosy. Interestingly, early research using thermography in leprosy confirmed the presence of *M. leprae* in the cooler parts of the body by thermography.<sup>52,53</sup> The mentor of preventative rehabilitation in leprosy, Paul Brand, used IRT a few decades ago to show that increased temperatures preceded skin breakdown.<sup>52–55</sup>

Notably, the study by Balagon *et al.* involved patients using a *self-assessment* tool. An essential part of this tool was asking patients to observe *inflamed* skin lesions. When located in the vicinity or overlying a nerve, these were considered to put the nerve at risk.<sup>31</sup>

In 2007, an internationally developed consensus workshop reviewed neuropathology, leprosy diagnosis, neurological assessment, and treatment. Given recent developments in evaluation and insights into prevention and treatment, an update to this important document is warranted.<sup>56</sup>

Table 2. Infrared thermography (IRT) studies in leprosy

| Authors      | Title                                                                      | Ref. | Study subjects                       |                    |                                              | Temperature recorded by   | Results                                                        | Comments                                              |
|--------------|----------------------------------------------------------------------------|------|--------------------------------------|--------------------|----------------------------------------------|---------------------------|----------------------------------------------------------------|-------------------------------------------------------|
|              |                                                                            |      | A<br>Leprosy                         | B<br>Non-leprosy   | C<br>Non-Leprosy                             |                           |                                                                |                                                       |
| Cavalleheiro | 2016<br>Thermographic analysis of autonomic function following cold stress | 19   | Heterogeneous on treatment<br>N = 17 | N = 15             |                                              | FLIR camera               | See Table                                                      | Hands tested following cold spray                     |
| Tiago        | 2021<br>Assessment of neuropathic pain (NP)                                | 35   | N = 55<br>29 with, 26 without NP     | N = 20             |                                              | Digital thermo-hygrometer | Compared to controls all patients showed temperature asymmetry | Neuropathic pain not defined<br>Hands and Feet tested |
| Sabino       | 2023<br>Evaluation of skin temperature in hands                            | 47   | N = 48 on treatment                  | N = 22             |                                              | FLIR                      | Increased asymmetry in leprosy MB > BT                         | Hands                                                 |
| Sabino       | 2024<br>Asymptomatic contacts                                              | 46   | None                                 | N = 23<br>Contacts | Seropos. = 66<br>Seroneg. = 55<br>No contact | FLIR                      | See Table                                                      | Hands                                                 |
| Vinay        | 2024<br>Use of cutaneous thermography                                      | 66   | Newly diagnosed<br>N = 5             | None               |                                              | FLIR                      | Sites of impaired sensation are cooler                         | Hands/feet                                            |

FLIR: Forward Looking Infrared.

Notice variability in the studies! See text for other than IRT studies of autonomic nerve function assessment in leprosy, none of which have been adopted in routine leprosy practice.

Many studies have been done in Diabetes (neuropathy) - See text

Little is known about the epidemiology of the diagnostic cardinal signs. Following further research, IRT could become a proper adjunctive technique in diagnosing or confirming the disease, for follow-up, and in the differential diagnosis. Some leprologists have been critical of relying solely on the three cardinal signs and suggested that two additional signs—ulnar nerve enlargement and sensory loss of the palms of the hands and soles of the feet—could be added to increase the validity of the diagnosis.<sup>26,27</sup>

Nerves may be palpable and found enlarged or tender. However, the lack of expertise in nerve palpation among primary healthcare workers in integrated health services and medical officers not trained in leprosy often renders the diagnosis inconclusive.

Potentially, IRT could be used to monitor the temperature of the nerves. When these are enlarged and inflamed, this may be reflected in the skin temperature overlying the nerve. This is particularly applicable to the commonly affected nerves, including the ulnar, median, common peroneal, and posterior tibial nerves.

Thermography can detect abnormal surface temperatures without the cardinal signs, especially in contact examinations of patients with lepromatous leprosy.<sup>40–44</sup> If found, prevailing policies should determine advice. Should subjects be reviewed after a given time? Should prophylactic treatment be given?<sup>57</sup>

Of course, age- and gender-specific normative and cut-off values should ideally be known, and more research is needed in this area. However, significant left-right differences could already be essential in decision-making and policy.

The reliability of somatic, sensory, and motor functions in leprosy has been assessed.<sup>9,10</sup> To date, no information exists regarding the reliability of IRT assessments in leprosy, unlike in diabetes, where several studies have been conducted.<sup>28,29,58,59</sup>

In leprosy, loss of autonomic nerve function is assumed when sensory loss is present. But if there is evidence that early sympathetic nerve function precedes sensory/motor loss, should there not be an inexpensive and practical way to determine autonomic nerve function loss? *“The advantage of infrared thermography is that it is a fast, non-contact, painless, side-effect-free, and non-observer-dependent diagnostic and evaluation tool.”*<sup>59</sup>

Our research group is currently investigating the use of IRT through a small infrared video camera attached to a mobile phone, where dynamic video recordings, following cold stress testing, can be analyzed to gain more insight and answers to some questions raised in this paper.<sup>60</sup>

Neuropathy in diabetes predominantly affects the lower extremities, whereas leprosy neuropathy may result in neuropathy affecting both upper and lower limbs. Studies in diabetes confirm that early impairments of autonomic nerve function may indicate the development of clinical diabetes and “manifest” sensory loss.<sup>28,29</sup>

Ultrasound examination could also be helpful in the differential diagnosis and in selected subjects where the diagnosis is doubtful, such as in cases of neural leprosy. Few studies have been conducted using ultrasound (US) in the treatment of leprosy.<sup>61–64</sup> Can IRT complement the diagnosis of neural leprosy to provide a better understanding of nerve pathology and assess treatment efficacy, whether medical or surgical? Ultrasound examinations would be potentially more informative about structure, whereas IRT could be more informative about function.

Besides ultrasound and electro-neurophysiological techniques, with further research, infrared thermography has the potential to become a valuable and affordable tool in the diagnosis of leprosy and the assessment and follow-up of its major complications, including neuropathy and its consequences.



## Conclusions/recommendations

Several studies have shown that early loss of autonomic nerve function may precede impairments in somatic nerve function: sensation (touch) and muscle strength. Early impairments in autonomic function, preceding somatic nerve changes in leprosy, have been shown in electrophysiological and infrared thermography studies. These impairments may indicate early progression to clinical disease and neuropathy. Further studies are warranted to assess the clinical applicability and reliability of autonomic nerve function evaluation in leprosy.

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