Materials and Methods

This study is part and an extension of a study from the "Tattoo Clinic" at the Department of Dermatology and the Wound Healing Centre of Bispebjerg University Hospital, Copenhagen, conducted from October 2008 to June 2015 [11]. In the present study, a total material of 406 patients with 494 tattoo complications was available for analysis. Of these, 92 papulo-nodular reactions in 72 patients were diagnosed. This group is supposed to include cases of sarcoidosis and sarcoid reactions and therefore differentiated into the subgroups *sarcoidosis* and *non-sarcoidosis*, depending on histopathological findings and sarcoid manifestations (see Fig. 1). The association between gender, tattoo size, and number of tattoos was explored.

The papulo-nodular pattern is diagnosed according to clinical examination showing papules or nodules or both variably distributed in the tattoo and typically confined to the problem colour, which is typically black. Manifestations are severe in heavily coloured parts of the tattoo, which may be "overdosed" and visibly saturated with pigment *(pigment overload)*. Histology typically shows high pigment density and possibly large agglomerates or clusters of pigment. Papules and nodules may have the histology of plain inflammation, granulomatous inflammation, or *sarcoid granulomas*, the latter pattern also being associated with inflammation. Sarcoid granulomas require the presence of epithelioid cell granulomas, typically without necrosis but with giant cells and epithelioid cells, and with inflammation. Findings by histology with a sharp distinction between the groups, according to assessments by the pathologists, are difficult.

Sarcoidosis, Diagnostic Entities, and "Rush Phenomenon"

In the case of sarcoid granulomas by histology, the reaction was concluded as cutaneous sarcoidosis, and labelled *"sarcoidosis, cutaneous, tattoo only"* if no other manifestations occurred in the skin or systemically. Other manifestations of cutaneous sarcoidosis additional to sarcoidosis of the tattoo (i.e., sarcoidosis in scars and erythema nodosum) were diagnosed according to common standard and labelled *"sarcoidosis, cutaneous, tattoo and other".* Systemic manifestations in the lungs, the eyes, or joints etc., additional to sarcoidosis of the tattoo, were labelled *"sarcoidosis, systemic, tattoo and organ"* (Table 1).

A specialist of dermatology (J. Serup) examined all patients with complete and detailed patient history and clinical examination. The skin integument was routinely screened for any other manifestation of sarcoidosis. Observations were also structured into initial and subsequent manifestations. This included

secondary reactions appearing in other tattoos hitherto tolerated but becoming active *after* the initial tattoo started to react. We defined these secondary reactions of other tattoos as "*rush phenomenon".* Rush phenomenon, thus, was used to describe a special clinical observation when a newer black tattoo, the trigger, with papulo-nodular reaction preceded the development of similar reactions in any part of the skin affecting other black tattoos.

"Major rush phenomenon" is defined as a rush affecting many other black tattoos and *"minor rush phenomenon"* as a rush affecting only a few other tattoos and to a more limited extent. Rush phenomenon develops abruptly over a few days or weeks.

All patient data were collected from patient records and analysed (M. Sepehri and K. Hutton Carlsen).

In suspected organ involvement, chest X-rays (supplemented with high-resolution CT) and joint X-rays were performed, and relevant specialists including internists, ophthalmologists, and rheumatologists were consulted. Examination also included any other tattoo on the individual and any other skin pathology with emphasis on erythema nodosum, scar sarcoidosis, and other manifestations of the disease.

Biopsies and Histopathology

Punch biopsy was routinely performed on indications normally practised in the clinic (i.e., to support diagnosis and choice of treatment), dependent on the severity of the problem and the burden of disease. Biopsies were processed and evaluated by pathologists of the hospital, following their normal in-house standards and based on pattern recognition as described by Ackerman [12].