Microneedle Penetration and Puncture of a Model Soft Material

Steven J. Henry, Walter L. Brown, Ph.D., and Richard P. Vinci, Ph.D.
Bioengineering, Lehigh University, Bethlehem, PA 18015

Motivation

Drug delivery using a transdermal patch is painless and easy to self-administer, but large macromolecule therapeutic drugs such as insulin cannot pass through the skin.[1] Microneedles on the underside of a patch can break the outer skin barrier, enhancing drug transport without pain or bleeding. This approach has been demonstrated,[2] but as yet there is insufficient understanding of the conditions that cause skin puncture under small loads to guide microneedle design. A model of soft-solid puncture mechanics could serve as both an aid in the design of future transdermal drug delivery devices and as a mechanical assay of potential artificial skin analogs that would reduce the need for cadaver or *in vivo* testing.

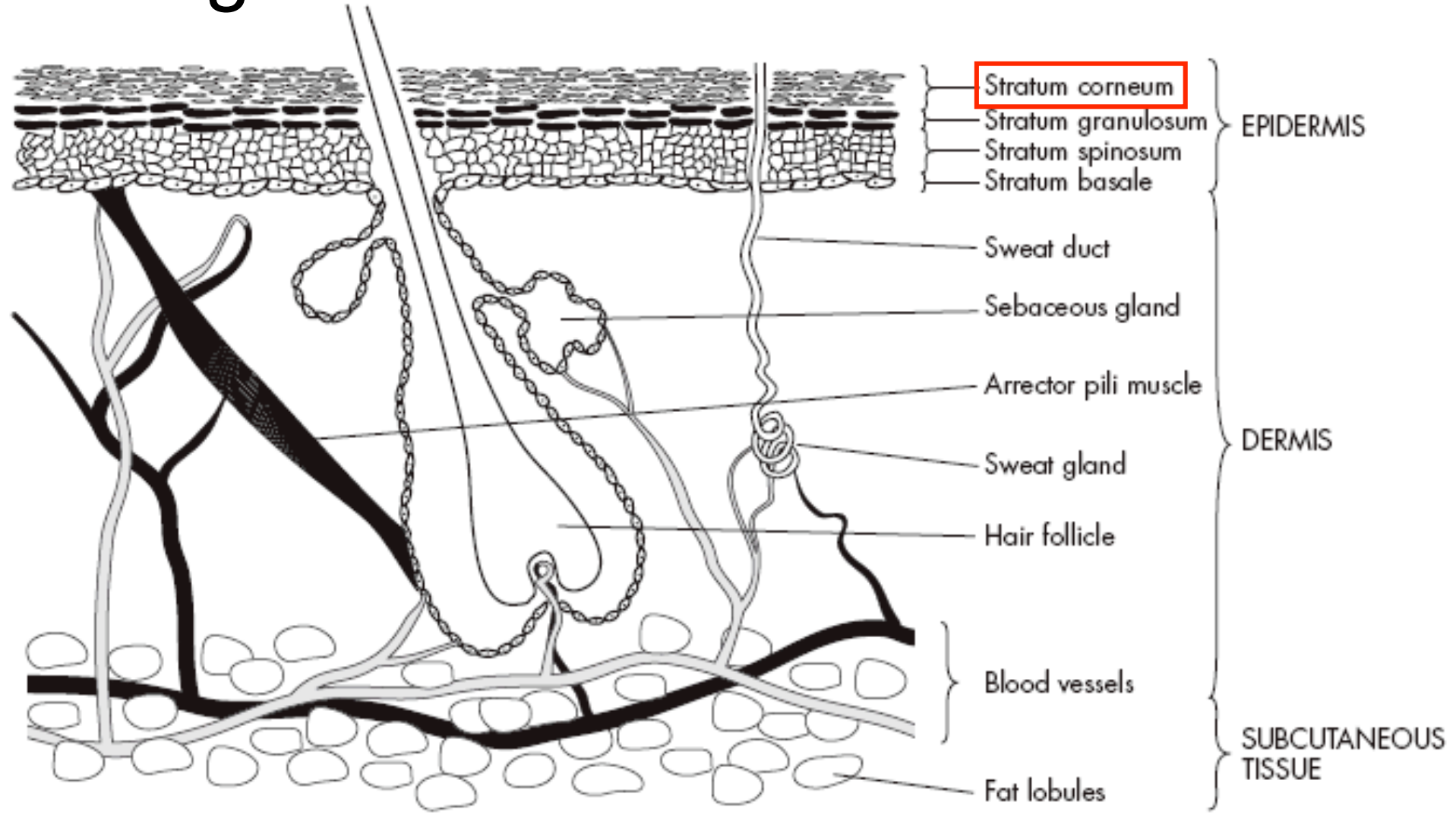

Figure 1 Diagrammatical cross section of human skin. The stratum corneum is the principle barrier to drug delivery (average thickness of 10 μm). [3]

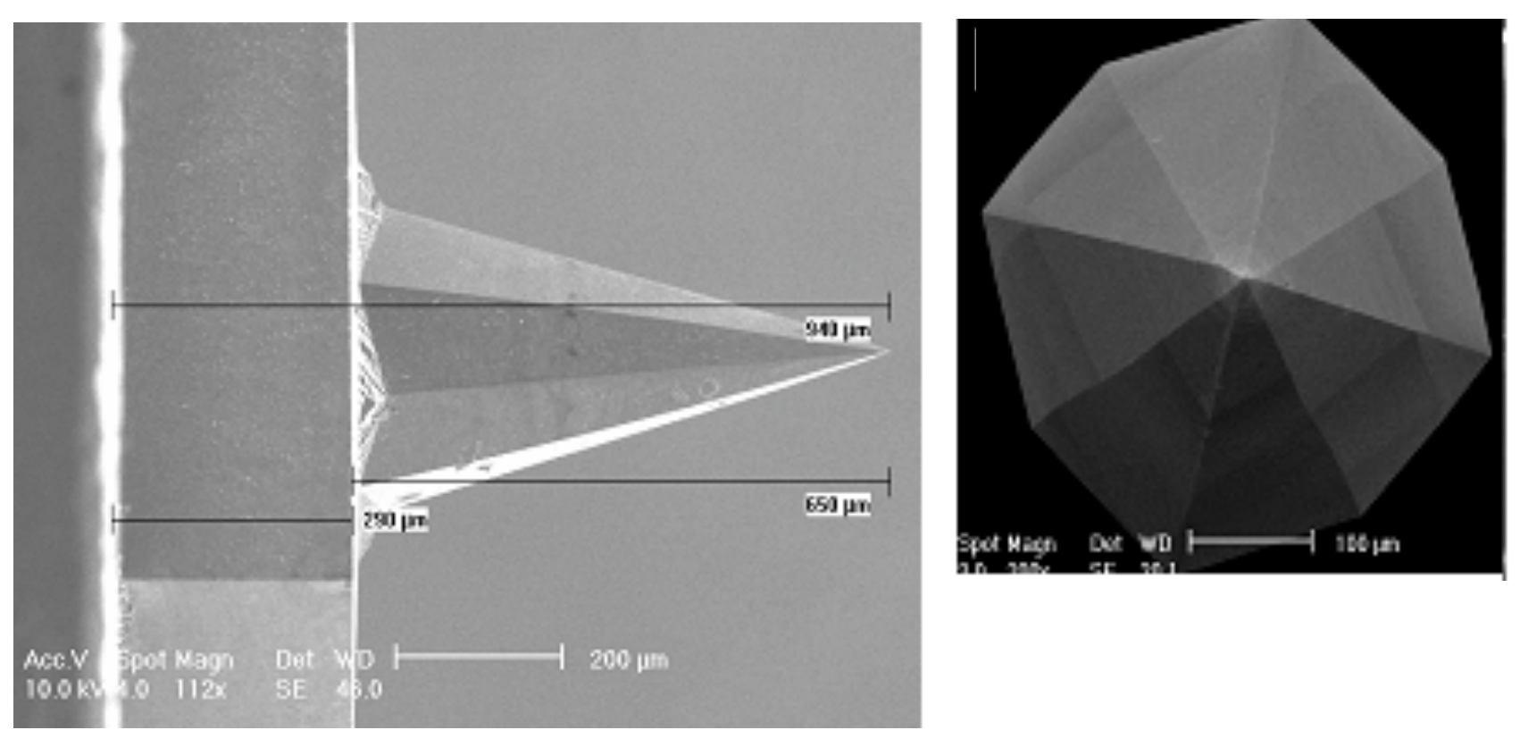

Figure 2 SEM profile (left) and plan view (right) of a commercially produced solid, conical, octagonal, silicon microneedle.[4]

Goal

The long term vision is to develop and validate a model of microneedle penetration and puncture of a polymer that has similar mechanical properties as human skin. To this end an investigation into the role of tip half-angle on required puncture force was undertaken.

Approach

Materials: A test apparatus, consisting of a load cell and a stepping-motor/micrometer combination, was constructed. It enables the user to monitor applied force and displacement while a microneedle contacts, penetrates, and punctures a soft substrate. SYLGARD® 184 Silicone Elastomer polydimeythlsiloxane (PDMS) polymer was selected as the substrate because of its homogenous and highly elastic nature. It is also transparent which facilitated *in situ* observation of sub-surface test events. Stainless steel conical microneedles of 0.125 in diameter were fabricated with half-angles ranging from 12° to 64°. Average tip radius was approximately 2 μm. The needles were macroscopic in scale but had tip angles and sharpness close to those of actual microneedles.

Protocol: Microneedles were mounted normal to the PDMS specimen and moved along the normal axis toward and into the substrate at a constant rate of 0.10 mm/s until a specified maximum load was reached and withdrawal initiated at the same rate. In this experiment needle half-angle was varied. The basic data output generated was load as a function of needle displacement.

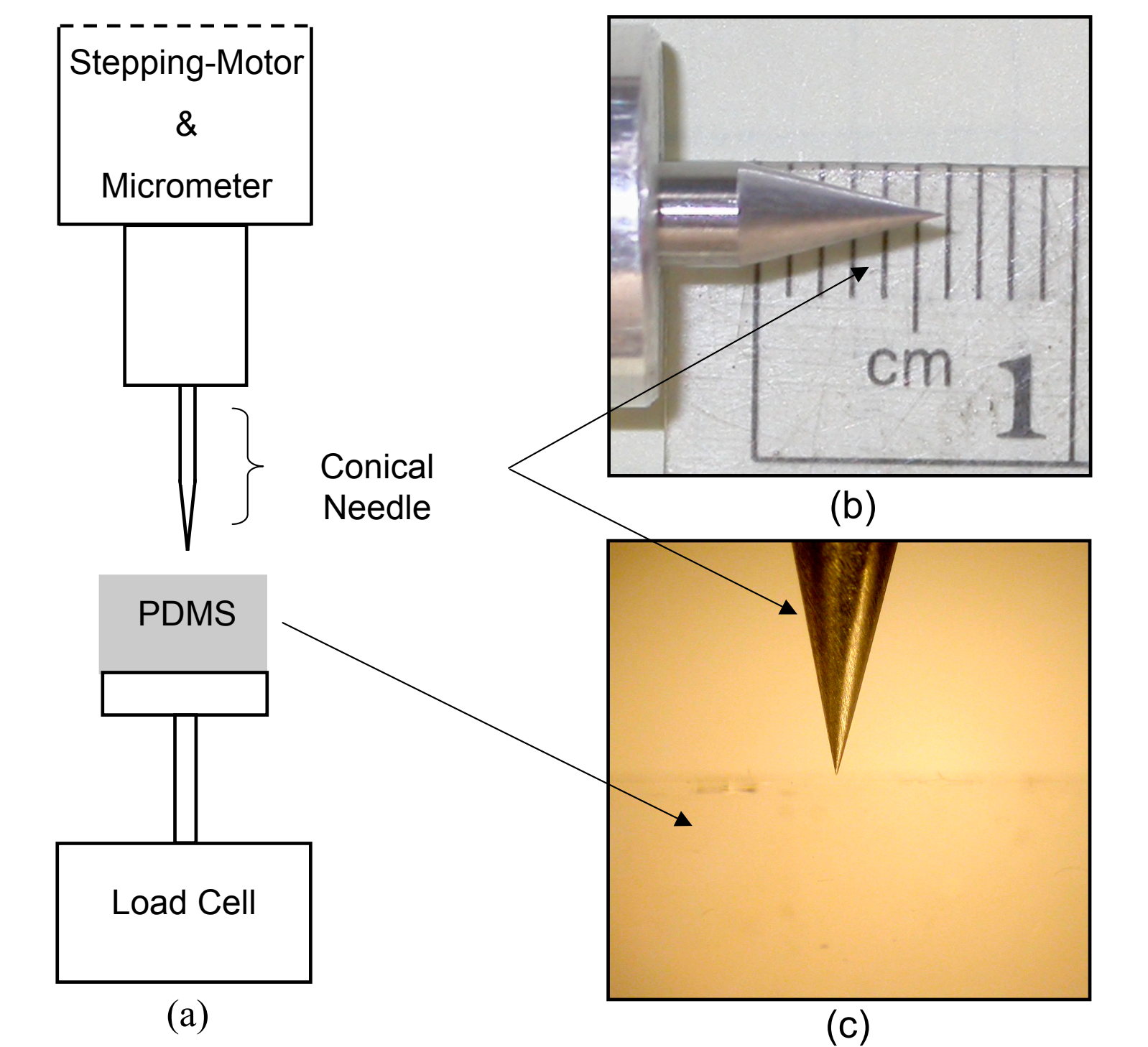

Figure 3 (a) Schematic representation of the experimental test apparatus comprised of a load cell and stepping-motor/micrometer combination. (b) Solid conical stainless steel needle of 0.125 in diameter and approximately 15° half-angle. (c) Needle tip positioned approximately normal to polydimethylsiloxane (PDMS) substrate prior to penetration cycle.

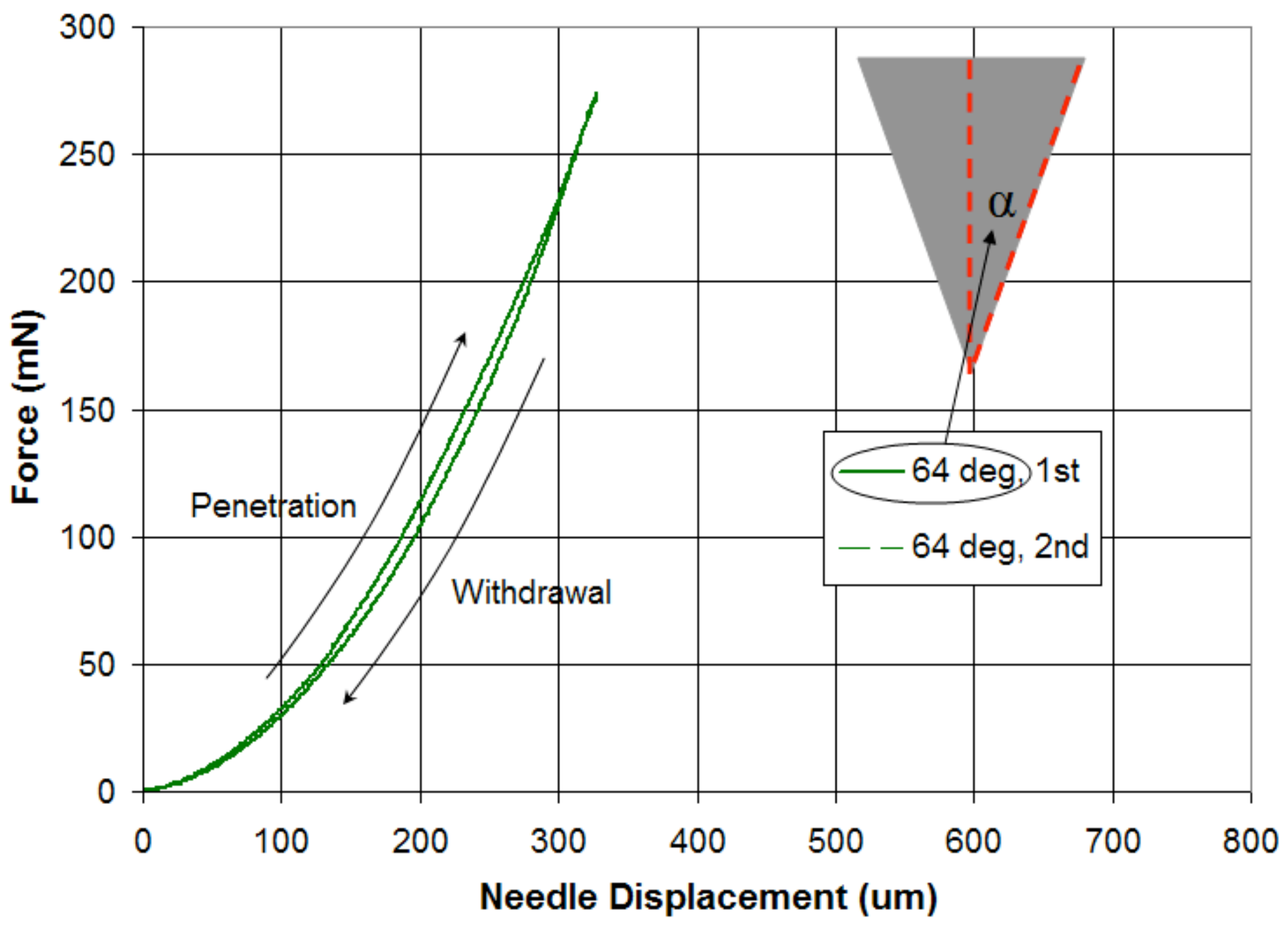

Figure 4 Typical load vs. needle displacement data for a large half-angle microneedle. As the needle advanced into the material the applied force simultaneously increased to a maximum level. Penetration was halted and withdrawal initiated at the same rate as penetration. This plot shows penetration but not puncture, as confirmed via energy loss analysis and stereomicroscopy (discussion of which follows). A small energy loss (hysteresis) is attributable largely to the viscoelastic nature of the PDMS. A second penetration and withdrawal cycle in the same location as the first is not visible as it is exactly superimposed upon the results of the first cycle.

Results

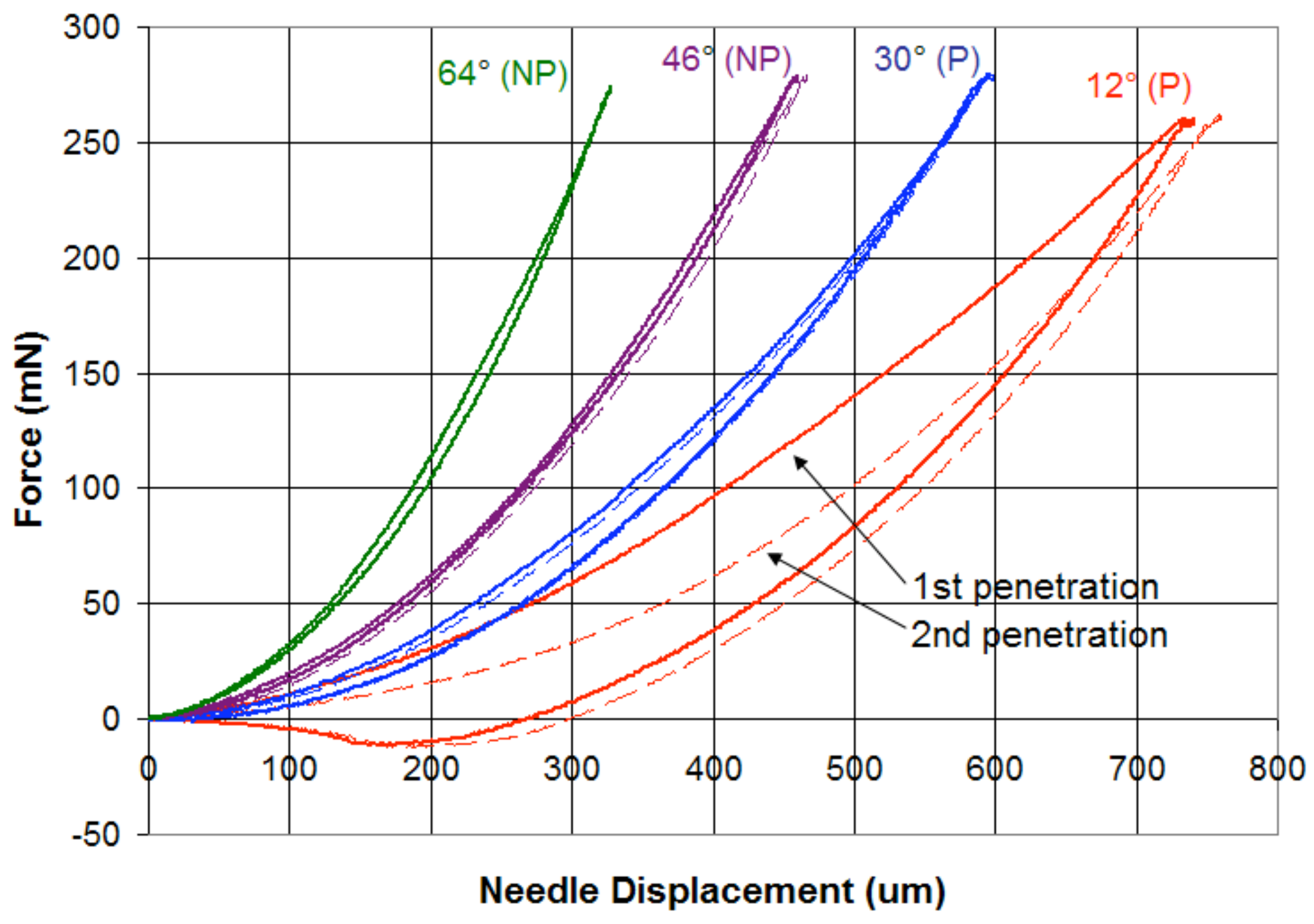

Figure 5 Selected results of variable half-angle penetration and withdrawal load vs. needle displacement tests. As needle half-angle decreases: (1) depth of penetration increases, (2) the size of the hysteresis loop increases, and (3) the difference in the shape and position of a second penetration and withdrawal cycle compared with the first becomes more pronounced.

With decreasing microneedle half-angle, the size of the hysteresis loop increases and the difference in shape and position of a second penetration and withdrawal cycle compared with the first becomes more pronounced. Our hypothesis was that such differences were the result of puncture in the material, the extent of which is a function of needle half-angle. Two avenues of verification where pursued:

(1) visual confirmation of puncture
(2) energy loss quantification

Visual Confirmation

Transparency of the PDMS substrate facilitated stereomicroscopic observation of penetration and withdrawal. Surface puncture was confirmed by observation of a puncture cavity upon microneedle withdrawal. Presence or absence of such a cavity was correlated to each penetration and withdrawal cycle of Figure 5 above. "P" denotes puncture. "NP" denotes no puncture.

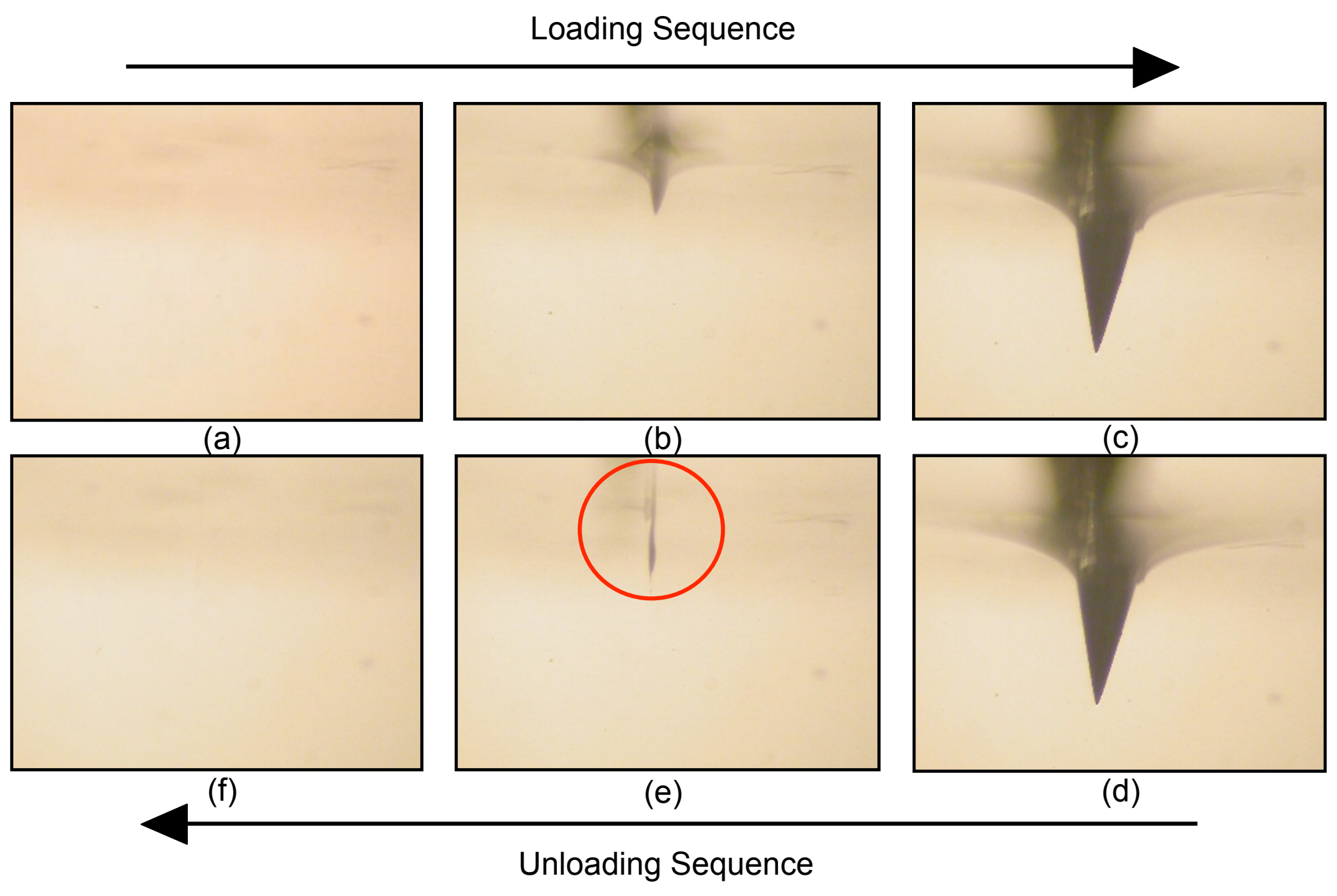

Figure 6 Photographs of a representative penetration and withdrawal sequence conducted in PDMS. The sequence consists of (a) pre-needle contact (b) needle contact and continued penetration (c) maximum penetration reached and penetration halted (d) withdrawal initiated (e) complete needle removal, residual puncture cavity remains (f) puncture cavity closes completely.

Energy Loss Quantification

Numerical integration of each penetration and withdrawal cycle was performed to quantify the extent of energy loss as a function of microneedle half-angle. First and second penetration energy losses converge to a constant energy loss at half-angles greater than 32° ± 1.5º. These results are consistent with those of the optical verification method above.

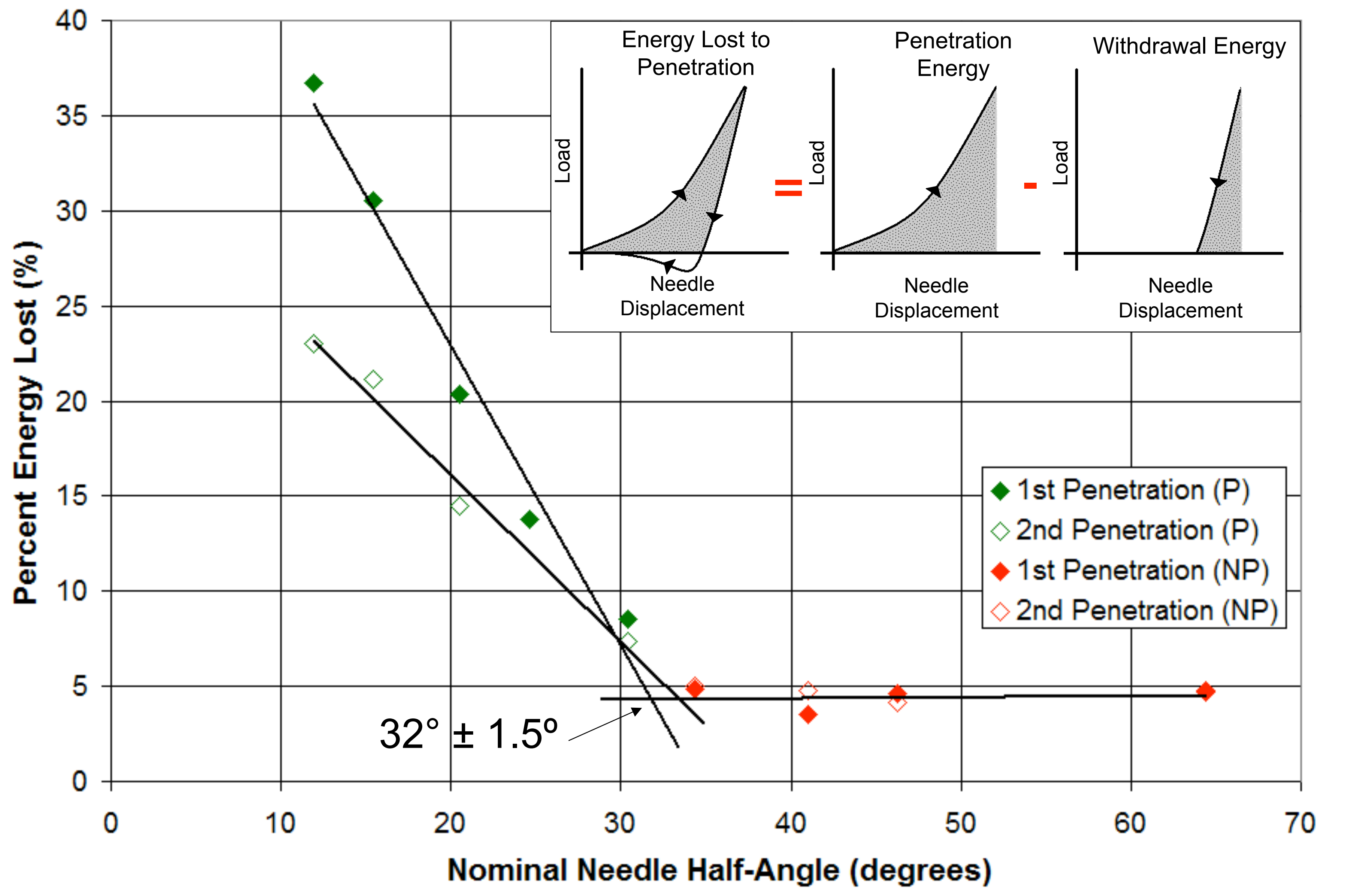

Figure 7 Two regimes of energy loss emerge: a constant loss for larger half-angles and a changing loss for smaller half-angles. First (solid diamonds) and second (open diamonds) penetration energy losses have different slopes. Linear fits to the three segments converge at approximately 32° ± 1.5º. This critical angle between puncture and lack of puncture correlates with visual evidence of puncture cavities for the needles of 30° half-angle and smaller. P denotes puncture (green). NP denotes no puncture (red).

Conclusions

- Puncture verification may be achieved via quantification of hysteretic behavior in load versus displacement of first penetration and withdrawal data without a second test or visual observation.
- There is a clear dependence of puncture event on microneedle half-angle.
- Half-angle is a key microneedle design criterion.

References

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