



FIGURE 4 Mechanical stresses inside an axially symmetric glass body.

(Fig. 4). In contrast to σ_{rad} , tangential stresses σ_{tan} are tensile and can induce critical stresses on surface defects (15):

$$\sigma_{tan} = \frac{p_{hyd}R}{t} \quad (6)$$

where p_{hyd} is the hydrostatic pressure, R is the radius, and t is the wall thickness of the glass container. The values of axial stresses σ_{ax} can be estimated by (15)

$$\sigma_{ax} = \frac{p_{hyd}R}{2t} \quad (7)$$

Equations (6) and (7) are valid for thin-walled containers only. It is obvious from equations (5) to (7) that in a glass body with rotational symmetry the tangential stresses are the most critical stresses determining the fracture behavior. Since σ_{ax} is lower than σ_{tan} by a factor of 2, the direction of crack propagation of a vial at failure normally starts parallel to the axis before bifurcating (Fig. 6).

During the cooling step in the lyophilization process, the formulation freezes and starts expanding. Because of this expansion, radial stresses are applied to the inner wall of the vial, which involve tangential tensile stresses σ_{tan} . The hydrostatic pressure introduced by the burst-testing apparatus simulates the mechanical load of an expanding lyo cake during the cooling step. Thus, burst-pressure testing is a suitable technique to simulate the mechanical loads that appear during the freezing process and to investigate the stress distribution of the vial.

Vial strength (vial breakage) can also be determined qualitatively by simulating the freeze-drying process using sugar alcohols (e.g., mannitol) or protein formulations as a substitute for more expensive pharmaceuticals. With