Fracture healing includes a complicated series of events that must occur in order to restore the broken bone to its pre-injury condition. Fracture stability dictates the mechanical strain between fragments and determines the pathway of healing that will occur: primary (intramembranous) ossification vs. secondary (endochondral) ossification. The characteristic distinction between these two bone-healing processes is that a provisional callus forms in response to higher inter-fragmentary strain in an attempt to provisionally stabilize fragments in endochondral ossification. Pertinent to this study, cigarette smoking is known to increase the risk of fracture non-union. However, the mechanism by which cigarette smoking inhibits fracture healing and both bone healing pathways is unknown. Therefore, the objectives of this work were to establish a reproducible cigarette smoke exposure protocol to study primary and secondary bone healing pathways using a bilateral femur fracture model and determine whether cigarette smoke exposure has a differential effect on the two fracture healing pathways.

Forty-six male Sprague-Dawley rats were randomly designated to control or smoke-exposed groups. In order to study the two primary fracture healing pathways, all animals underwent iatrogenic bilateral femur fracture with one side fixed via intramedullary nail and the contralateral side rigidly fixed by compression plating. Smoke-exposed animals (n = 23) were subjected to daily one-hour smoke exposures, for one month preoperatively and one month postoperatively. Effects of smoke exposure on fracture healing were assessed using histology, micro-CT, and four point bend tests at 10-day, 1, 3, and 6-month time points.

Cigarette smoke appears to have a preferential effect on cartilage callus area in healing fractures as determined by the pathway of osseous healing; the greatest effect was observed at one month in fractures healing via endochondral ossification. Likewise, on analysis of calcified callus via micro-CT, abundant callus formation in the control nailed femurs was found in comparison to their smoke exposed counterparts, as assessed by the callus volume/bone volume (CV/BV) ratio. Smoke-exposed nailed femurs exhibited less calcified callus at one and three months compared to the controls, suggesting inhibition of cartilage callus calcification by smoke exposure. Bone remodeling appeared to be impaired in smoke-exposed animals, evidenced by six-month CV/BV ratios exceeding those observed in controls, regardless of the method of fracture fixation. Cigarette smoke exposure also appears to preferentially impair the acquisition of mechanical stiffness after fracture healing at the 6-month time point following intramedullary fixation.

Overall, this study demonstrates a preferential inhibitory effect of cigarette smoke on fracture healing via the pathway of endochondral ossification. Our animal model provides an opportunity to further study the mechanism of inhibitory effects of tobacco smoke on the pathways of bone healing and offers clinical relevance to orthopaedic surgeons, who may have to carefully evaluate different fracture treatment approaches for patients who are active smokers, given the selective impairment of fracture healing via the endochondral ossification pathway.