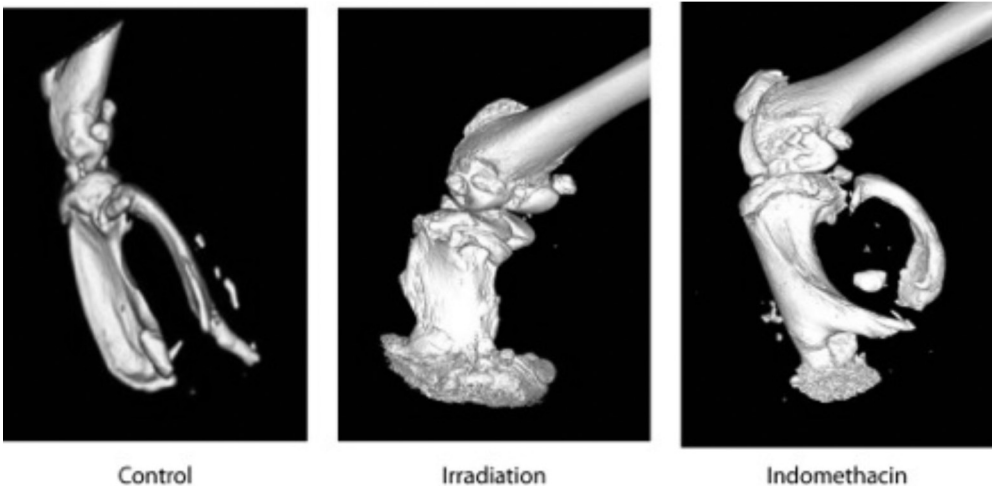


Failure of Indomethacin and Radiation to Prevent Blast-Induced Heterotopic Ossification in an Animal Model

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Purpose: Heterotopic ossification (HO) in the residual limb has been a common morbidity in soldiers who survive extremity amputation via blast mechanisms during recent war conflicts. While several Level I clinical studies have demonstrated the efficacy of prophylactic regimens using either nonsteroidal anti-inflammatory drugs (NSAIDs) or low-dose external beam irradiation (XRT) to prevent HO formation following total hip arthroplasty and surgical treatment of acetabular fractures, the HO prophylactic potential of any of these treatment modalities in the setting of trauma or trauma related amputation has never been assessed. This study was aimed at investigating the effectiveness of the NSAID indomethacin and irradiation, in the prevention of HO formation following extremity blast amputation in a rat model.

Methods: 36 Sprague-Dawley rats were subjected to blast amputation of a hindlimb via a column of propelled water following detonation of a submerged explosive. There were 12 controls, 12 animals received an oral suspension of indomethacin at a dose of 3 mg/kg for 10 days starting on operative day, while another 12 received a single dose 8 Gy of irradiation to the amputated stump on the third postoperative day. All wounds were treated with bulb syringe irrigation, minimal debridement of skin edges, and primary closure of fascia and skin. Serial radiographs were done until euthanasia at 24 weeks, at which time HO severity was quantified as (0) absent, (1) mild, (2) moderate, or (3) severe, and HO type qualified as contiguous with the residual stump or as distinct bony islands, by independent graders.



- The FDA has not cleared this drug and/or medical device for the use described in this presentation (i.e., the drug or medical device is being discussed for an "off label" use). For full information, refer to page 600.

Results: One animal in the irradiation group died 2 weeks postoperatively and was not replaced. One animal in the control and indomethacin groups, and 2 animals in the irradiation group developed persistent granuloma-like lesions on their residual stumps. These animals all had radiographic evidence of HO. The mean HO severity was 1.5, 1.14, and 1.97 in the control, indomethacin, and irradiation groups, respectively. The qualitative means of HO type were 1.5, 1.47, and 2.12 in the control, indomethacin, and irradiation groups, respectively. Kruskal-Wallis one-way analysis of variance revealed no significant difference in HO severity or type between both treatment groups and control.

Conclusion: While indomethacin and XRT used prophylactically have shown efficacy in the prevention of HO in non-blast extremity injuries, these interventions when administered in a similar fashion seem not to effect any change in the development of HO in the setting of blast-injured extremities with resultant amputation. This revelation may be indicative of the provocation of inciting stimuli so overwhelming that conventional interventions are ineffective. The effect of NSAIDs administered pre-blast, earlier XRT post-blast, or both treatment modalities combined immediately after blast injury warrants further study.