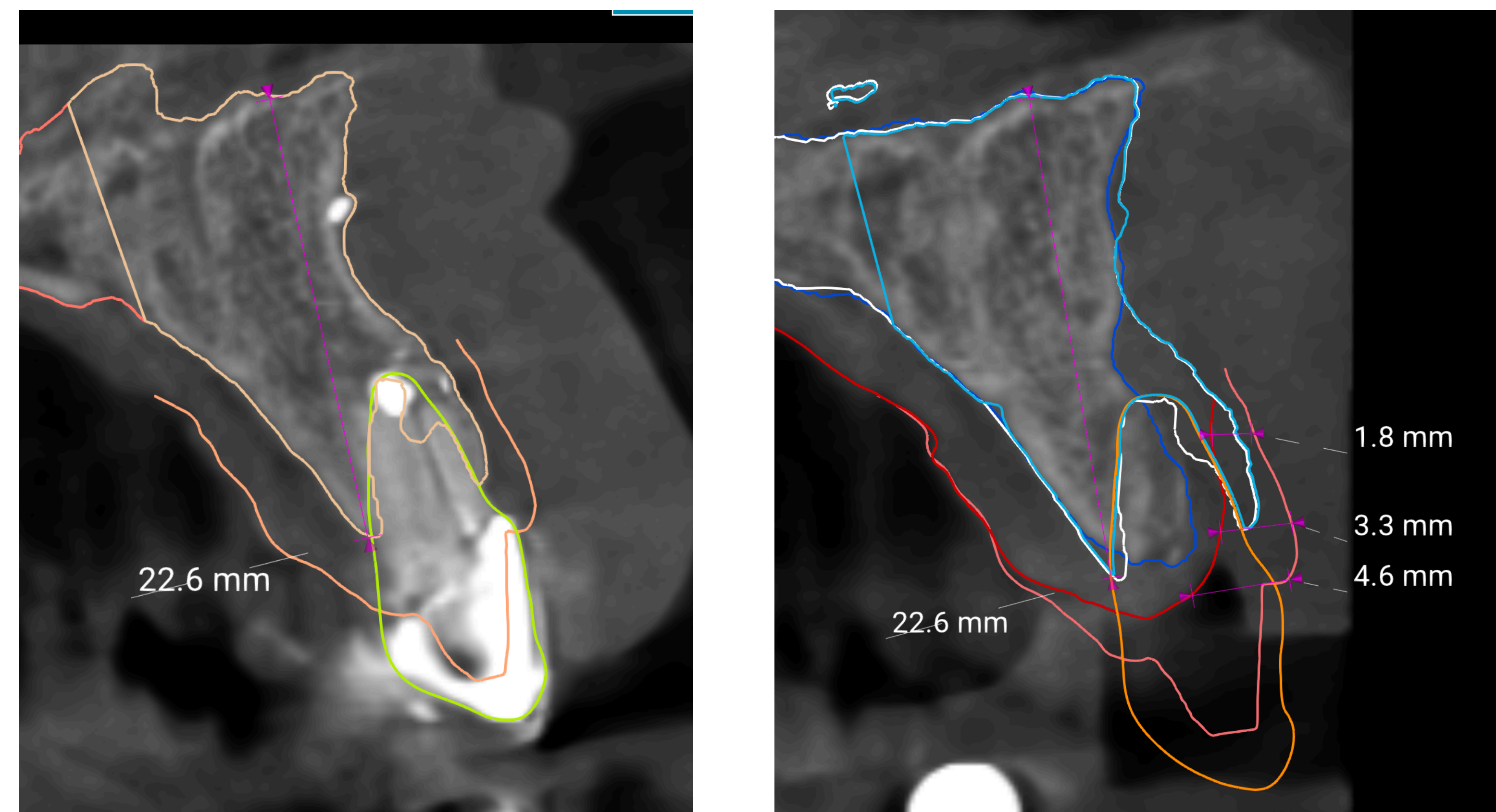
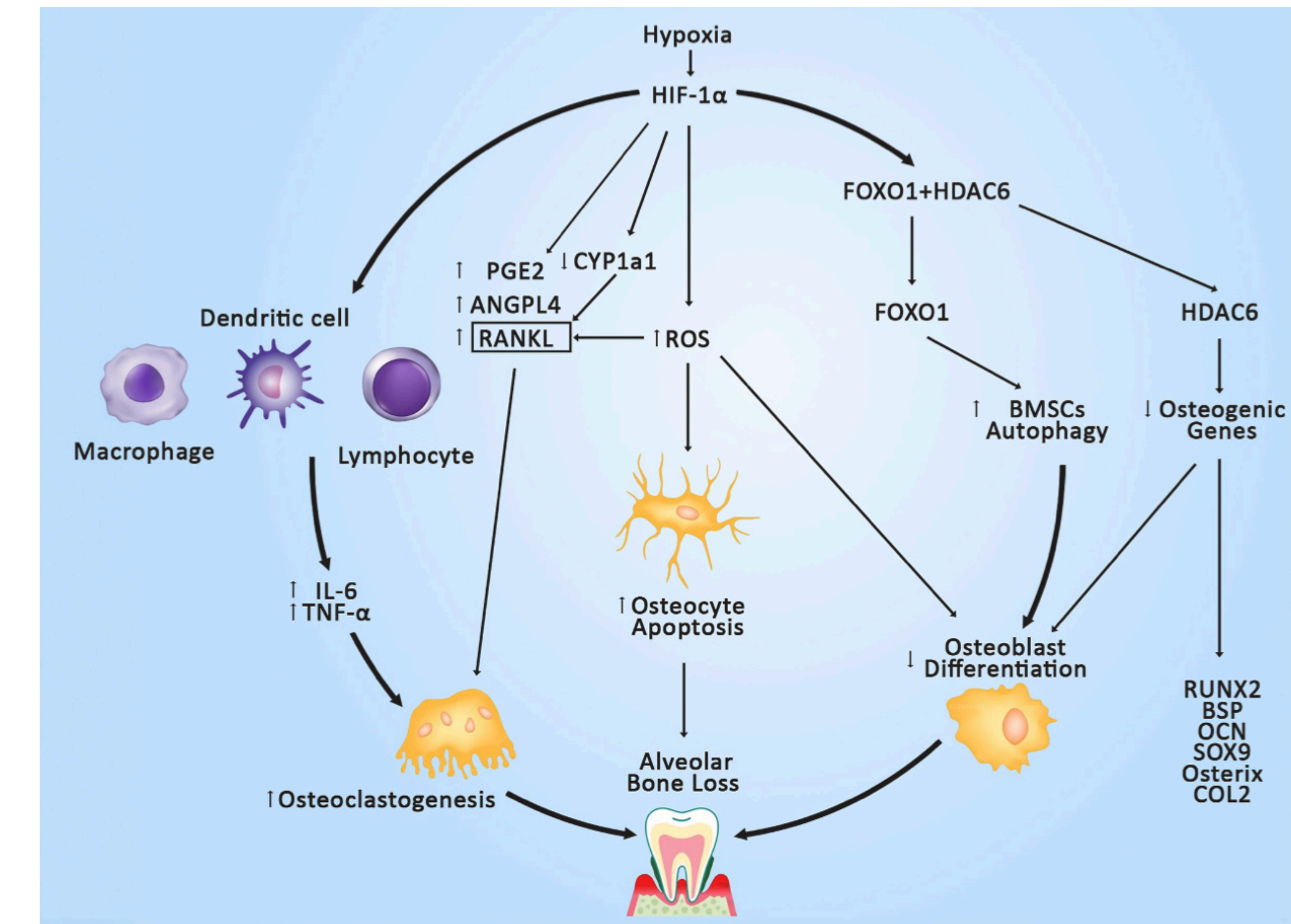


# Impact of Hypoxia on Alveolar Bone Healing in Immediate Implantology

Vatteroni Ernesto, Cosola Saverio, Menchini-Fabris Giovanni B., Toti Paolo, Piattelli Adriano, Covani Ugo, Romanos Georgios



Extraction  
& Implant



**Introduction:** Transient hypoxia has been shown to promote alveolar bone regeneration by activating hypoxia-inducible factors (HIFs), enhancing angiogenesis, and accelerating osteogenic differentiation.

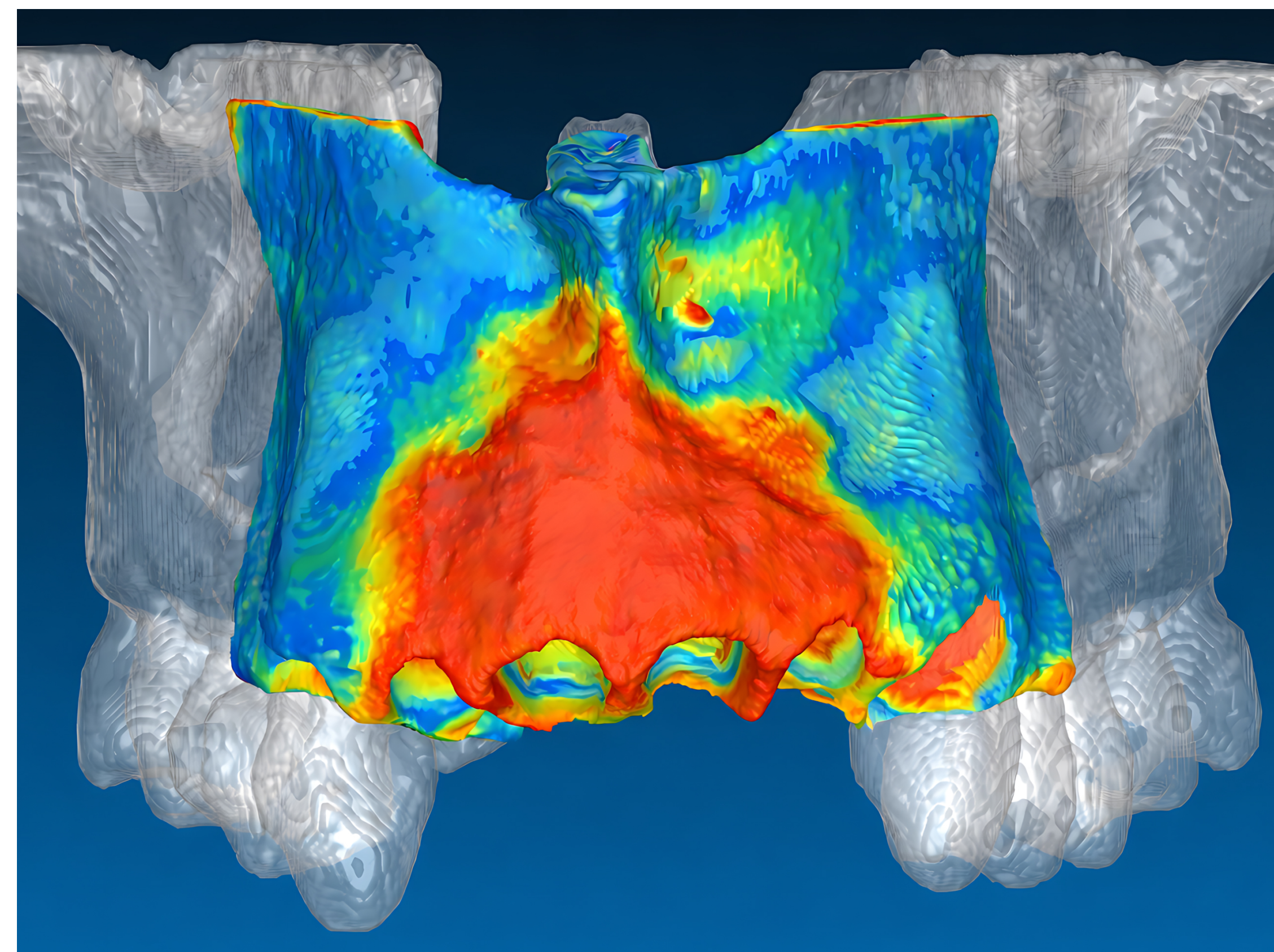
Immediate implant provisionalization clinically reproduces a controlled hypoxic microenvironment by sealing the post-extraction socket and limiting oxygen diffusion.

This study tests the hypothesis that transient hypoxia accelerates and enhances alveolar bone neoformation compared with normoxic delayed healing.



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**Method:** Evidence from preclinical models was integrated with a human retrospective clinical study involving 43 patients treated with immediate implant placement in the anterior maxilla. Patients were assigned to either an immediate provisionalization group ( $n = 24$ ), inducing controlled hypoxia through a tooth-like temporary crown, or a delayed loading group ( $n = 19$ ), allowing normoxic exposure via secondary intention healing.

Digital intraoral scans were taken at baseline and at 4 months.

Volumetric changes were calculated within a standardized 3D volume of interest (VOI), and soft tissue maturation was assessed using the Jemt Papilla Index.



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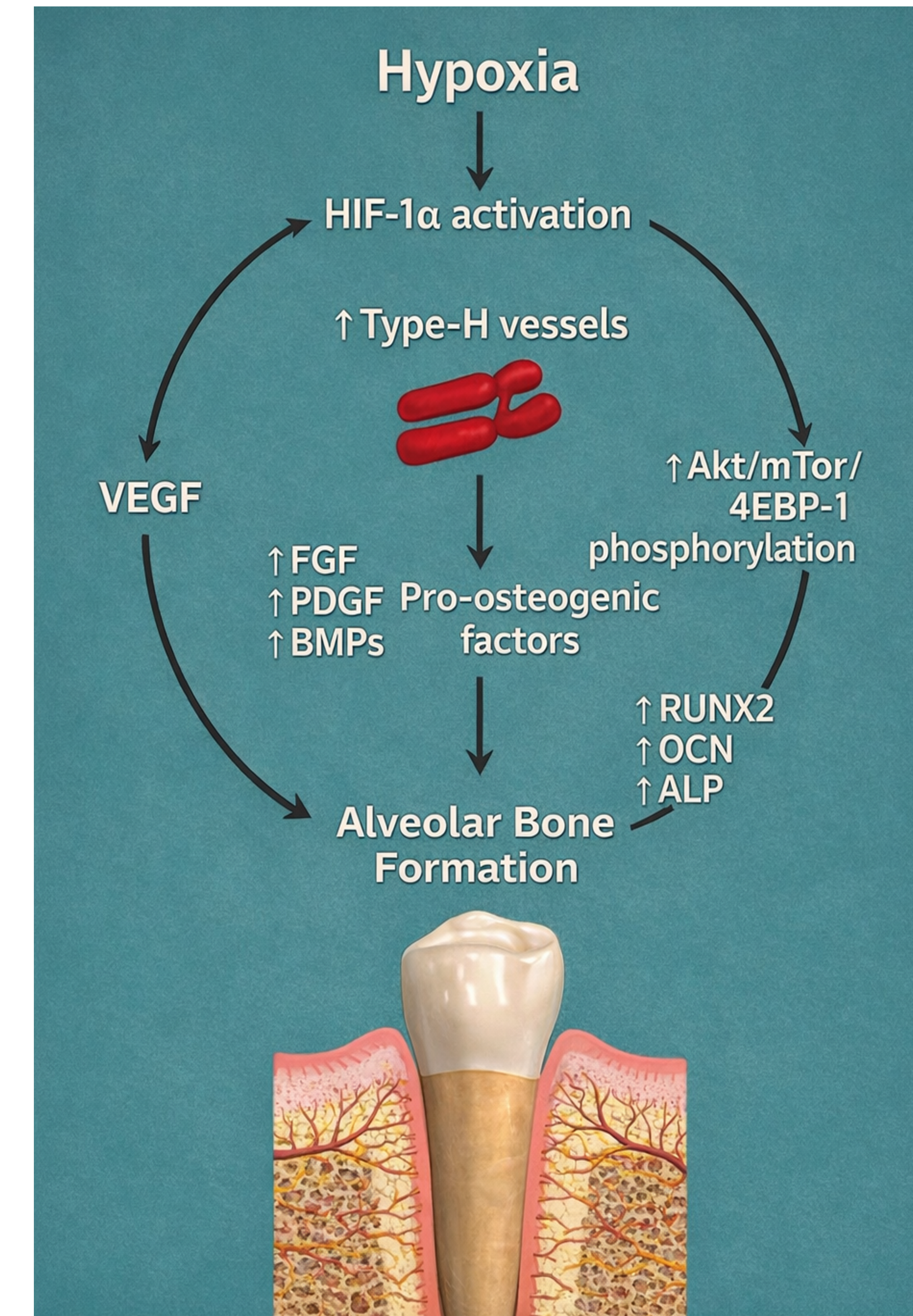
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## Preclinical Evidence

Preclinical investigations demonstrated that intermittent hypoxia significantly enhances regenerative signaling pathways. VEGF expression increased by up to 300%, indicating marked stimulation of angiogenesis. Concurrently, osteoblast differentiation was significantly enhanced, with a 2–3-fold upregulation of RUNX2 and osteocalcin expression. These molecular changes translated into accelerated socket mineralization and more rapid maturation of newly formed bone, supporting the hypothesis that transient hypoxic modulation actively promotes osteogenesis rather than merely preserving tissue volume.

## Clinical Outcomes

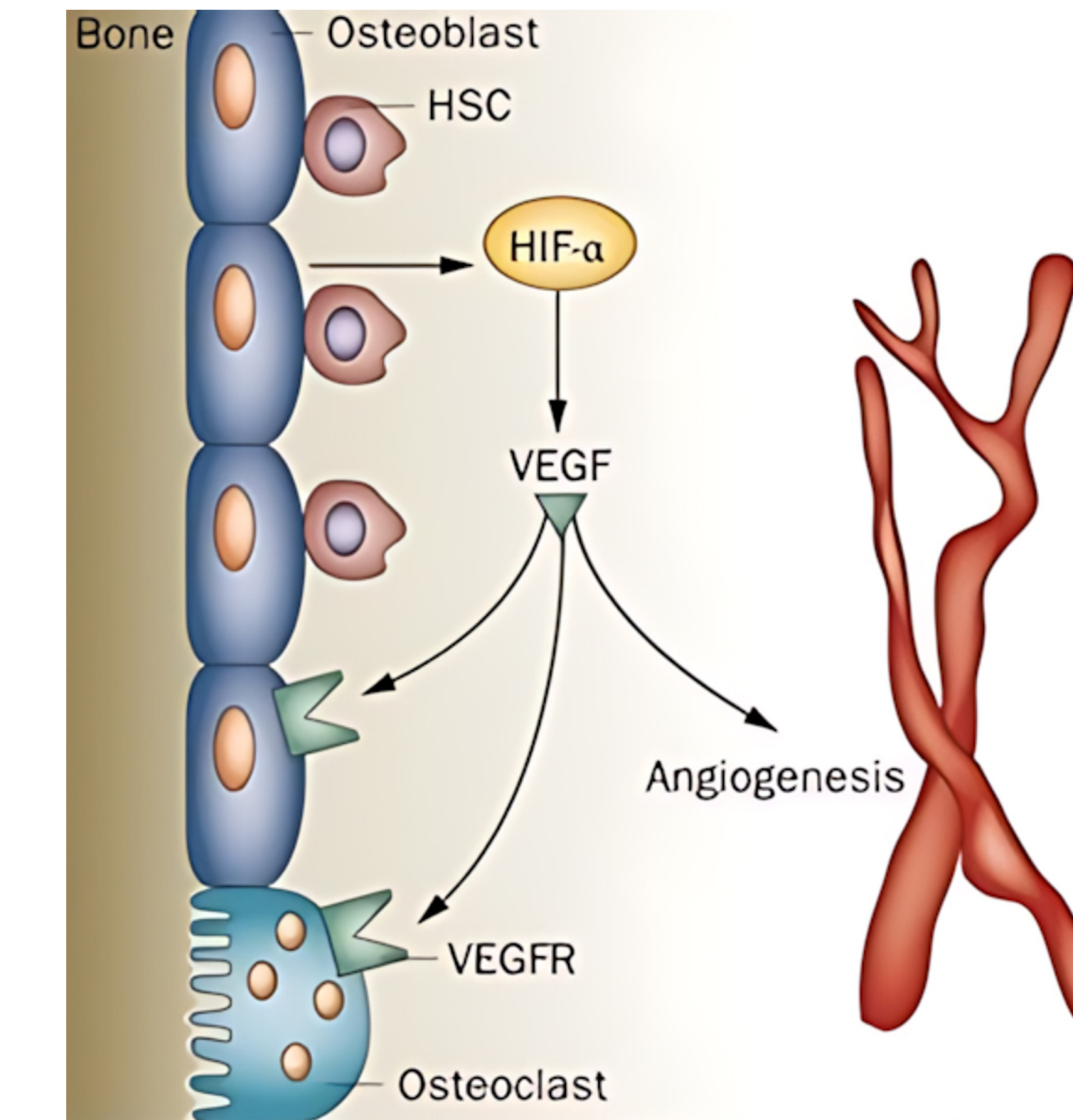
Clinically, alveolar volume loss was significantly reduced in the immediate provisionalization group compared with delayed healing. Mean volumetric reduction was  $-39 \pm 31 \text{ mm}^3$  in the immediate group versus  $-89 \pm 30 \text{ mm}^3$  in the delayed group ( $p < 0.0001$ ), corresponding to a 56% reduction in post-extraction volume loss. These findings indicate that immediate provisionalization substantially limits physiologic ridge remodeling.





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## Buccal Bone

Buccal volume loss was significantly lower in the immediate provisionalization group ( $-10.8 \pm 8.0 \text{ mm}^3$ ) compared with delayed loading ( $-16.5 \pm 6.9 \text{ mm}^3$ ).

Similarly, buccal area reduction was reduced ( $-7.5 \pm 4.8 \text{ mm}^2$  vs.  $-13.2 \pm 3.8 \text{ mm}^2$ ).

Given the critical role of the buccal plate in long-term esthetic stability, this reduction is clinically meaningful.

## Palatal Bone

Palatal volume changes were negligible in the immediate group ( $+0.7 \pm 5.0\%$ ), suggesting maintenance of tissue integrity and possible osteogenic activity rather than resorptive remodeling.

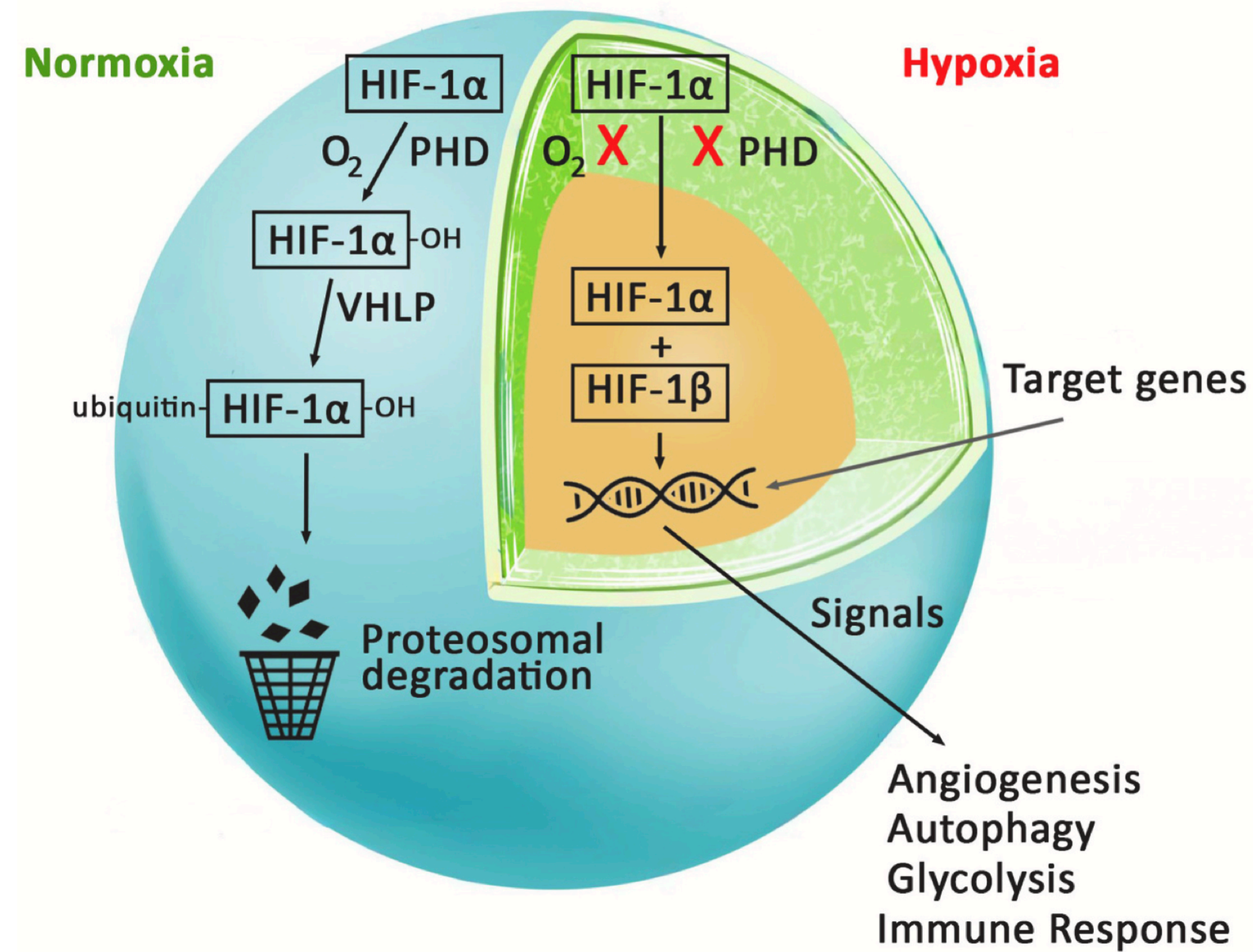
## Papilla Preservation

Interdental papilla scores were significantly higher in the immediate provisionalization group (mesial: 2.5 vs. 2.0; distal: 3.0 vs. 2.0;  $p \leq 0.005$ ), indicating superior preservation of peri-implant soft-tissue architecture.



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**Tooth extraction**  
Triggers hypoxia  
by disrupting  
blood flow in the  
alveolar socket.



**HIF-1α activation**  
Stabilized under  
hypoxic  
conditions,  
leading to VEGF  
expression.



**VEGF-driven  
angiogenesis**  
Promotes blood  
vessel formation  
for nutrient and  
oxygen delivery.



**Osteogenesis  
and bone  
remodeling**  
VEGF enhances  
osteoblast  
differentiation  
and supports  
bone  
regeneration.

## Biological Interpretation

Immediate provisionalization appears to function as a biologically active intervention. By sealing the extraction socket, it induces a controlled and transient hypoxic microenvironment. This condition activates HIF-1α-mediated pathways, promoting angiogenesis and osteogenesis and ultimately enhancing alveolar regeneration.

## Conclusion

Both molecular and clinical evidence support transient hypoxia as a biological trigger for alveolar bone neoformation. Immediate implant provisionalization should therefore be regarded not only as a volume-preserving strategy, but as an active regenerative stimulus.

Controlled hypoxic modulation may represent a paradigm shift in implant dentistry, redefining immediate provisionalization as a biologically driven regenerative approach rather than a purely prosthetic protocol.