

Proposed Mechanisms of FIR Therapy: Research Summary

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Sources of References: Lin CC et al 2007- 2013, Lai 2013, Yuen 2014

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A. Increased vasodilation and blood flow

1. Short-term thermal effect of FIR results in vasodilatation and increasing Qa. “According to the report by Hartel M et al, the temperature can be increased up to 4°C in 10 mm depth of tissue.” (1)
2. Energy transfer mechanism. “Multiple energy transfers as deep as 2–3 cm into subcutaneous tissue without irritating or overheating the skin like unfiltered heat radiation.” The skin temperature steadily increased to a plateau around 38–39°C during FIR treatment for 30– 60 minutes as long as the distance between the ceramic plate and the skin was more than 20 cm.” (Hartel M as quoted in (1))

B. Effects improving endothelial dysfunction

3. **“Long-term (accumulated thermal and non-thermal) effect of FIR therapy:** FIR may improve **endothelial function**, observed not only in animal studies, but also in one clinical study (Lin CC et al, 2007).” (3)
4. Yu SY et al: “Beneficial effect of FIR therapy on **skin blood flow** may be increased by FIR through activation of the **L-arginine/nitric oxide pathway.**” (1)
5. Akasaki Y et al found that “Repeated FIR therapy could **upregulate eNOS expression and augment angiogenesis** in an apolipoprotein E-deficient mouse model of unilateral hind limb ischemia.” (1)
6. “Ikeda Y et al reported that 4 weeks of sauna therapy **significantly increased serum nitrate** concentrations as well as the **expression of mRNA and protein of eNOS** in the aortas of TO-2 hamsters. (1)
7. Imamura M et al: “2 weeks of repeated sauna therapy **significantly improved vascular endothelial function, resulting in** an increase in flow-mediated endothelium-dependent **dilatation of the brachial artery from 4% to 5.8% in patients with coronary risk factors.**” (1)

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C. Potent anti-inflammatory anti-proliferative anti-oxidative effects: FIR induction of HO-1

8. **FIR activation of heme oxygenase 1 (HO-1)** “improves blood flow by inhibition of smooth muscle cells, platelet adhesion and vasospasm,” and with other mechanisms, “reduces oxidative stress” (4)

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9. Lin CC et al (2008): “Showed that far infrared therapy [FIR] induced expression of **HO-1 via stimulating NF-E2-related factor-2 (Nrf2)-dependent promoter activity**, with the maximal time-course effect on the expression of HO-1 and Nrf2 both at 6 hours.” (3)

10. Lin CC et al (2013 NDT):
“Concluded that: “FIR therapy can improve the function of AVF in HD patients, with the **best protective effect in those with S/S genotype of HO-1.**” (5)

11. Lin CC et al (2008) demonstrated that:
“Tumor necrosis factor- α (**TNF- α)-induced expression of E-selectin**, vascular cell adhesion molecule-1 (**VCAM-1**), and intercellular cell adhesion molecule-1 (**ICAM-1**) were maximally suppressed **by FIR therapy** at 4, 6 and 24 hours, respectively. **Higher expression of HO-1 may explain the antiproliferative and antiinflammatory effect of FIR therapy.**” (3)

12. Kipshidze N et al: “Nonablative infrared laser therapy **inhibited neointimal hyperplasia** after PTCA (percutaneous transluminal coronary angioplasty) in cholesterol-fed rabbits for up to 60 days due to **suppression of the growth of VSMCs.**” (1)

13. Masuda A et al (2004):
“Patients receiving FIR dry sauna for 45 minutes a day for 2 weeks **had lower systolic blood pressure and urinary levels of 8-epi-prostaglandin F 2α** , which is a chemically stable product of lipid peroxidation, and the level has been suggested [Patrono C. et al (1997)] to be **a reliable marker of oxidative stress *in vivo*.**” (1)

D. Mechanisms in the Context of improving AVF and AVG function in Hemodialysis

1. “Because HD patients are exposed to heavy oxidative stress from both inward uremic status and outward HD –related technology, the application of FIR therapy may be considered as an alternative therapeutic modality for decreasing oxidative stress.” (1)

2. “Apart from the previously mentioned nonthermal mechanisms (improving endothelial dysfunction, inhibiting neointimal hyperplasia, and lowering level of oxidative stress), one possible explanation of the higher unassisted patency of our patients may be an increase of the access flow after one year of FIR therapy.” (1)

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3. “In conclusion, FIR therapy, a noninvasive and convenient therapeutic modality, can improve Qa, inflammatory status and survival of the AVF in HD patients through both its thermal and the above mentioned non-thermal (anti-inflammatory) effects by **upregulating Nrf2-dependent HO-1 expression, leading to the inhibition of E-selectin, VCAM-1 and ICAM-1 expression.**” (3)

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4. Yueh FR et al 2014:

“RESULTS: Findings of this systematic review show that FIR interventions improve blood flow to and from the AVF and that the intervention decreases AVF malfunctioning...” FR Yueh (6)

“CONCLUSIONS and IMPLICATIONS FOR PRACTICE:

The results of the current study support the ability of patients with FIR to improve their AVF functions as well as the immediate clinical applicability of the suggested intervention. Although current empirical evidence supports the effectiveness of gripping a ball in maintaining AVF functions, many hemodialysis patients, due to age or illness, are not physically capable of doing this exercise. Therefore, FIR is a very good alternative measure.” Yueh FR (6)

5. “FIR therapy was also shown to improve access flow (Qa). The study by Lin et al – which was one of the RCTs included in the review - showed that 40 min of FIR therapy in a single HD session could increase access flow of AVF by about 50 mL/min with a 1-year effect of improving Qa by up to 150 mL/min and increasing unassisted patency of AVF by about 18% in comparison with controls” Bashar K (7)

6. Lai et al 2013:

“**Discussion... Four major findings:**

(a) AVF and AVG that have required more than two PTAs have very poor unassisted 1-year patency rates;

(b) Post-PTA FIR radiation therapy significantly improves the unassisted patency at 1 year compared with the usual form of radiation therapy;

(c) The use of FIR radiation improves the unassisted patency rate in patients with AVG but not in patients with AVF who have previously undergone more than two PTA;

(d) Post-PTA FIR radiation therapy particularly benefits AVG patients with age exceeding 70 years, no diabetes, fewer previous PTA, and non-occlusion type.”

7. Lai et al 2013: “**Conclusion:** The data show that post-PTA FIR radiation therapy is safe and effective, and improves PTA-free HD access patency, especially in the AVG series. This study suggests that this form of radiation therapy may be regarded as a helpful tool after PTA in terms of prolonged unassisted patency.”

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E. Sources of Quoted References

- (1) Lin CC, Chang CF, Lai MY, Chen TW, Lee PC, Yang WC. (2007)
Far-infrared therapy: a novel treatment to improve access blood flow and unassisted patency of arteriovenous fistula in hemodialysis patients. *Journal of The American Society Of Nephrology*. 2007 JASN, 18(3), 985-992.
- (2) Lin CC, Liu XM, Peyton K, Wang H, Yang WC, Lin SJ, Durante W. (2008).
Far infrared therapy inhibits vascular endothelial inflammation via the induction of heme oxygenase-1. *Arteriosclerosis, Thrombosis, and Vascular Biology* 2008. 28(4): 739-745
- (3) Lin CC and Yang WC (2009)
Prognostic Factors Influencing the Patency of Hemodialysis Vascular Access: Literature Review and Novel Therapeutic Modality by Far Infrared Therapy
J Chin Med Assoc. 2009 Mar;72(3):109-16. doi: 10.1016/S1726-4901(09)70035-8.
- (4) Lin CC, Yang WC, Chen MC, Liu WS, Yang CY, Lee PC (2013 AJKD)
Effect of far infrared therapy on arteriovenous fistula maturation: An open-label randomized controlled trial. *Am J Kidney Dis*. 2013. 62(2):304-311.
- (5) Lin CC, Chung MY, Yang WC, Lin SJ, Lee PC. (2013 NDT) **Length polymorphisms of heme oxygenase-1 determine the effect of far-infrared therapy on the function of arteriovenous fistula in hemodialysis patients: A novel physiogenomic study.**
Nephrol Dial Transplant. 2013 May; 28(5):1284-93.
- (6) Yueh FR, Ko NY, Yen M [The Effectiveness of Far-infrared Therapy in Hemodialysis Patients With Arteriovenous Fistula: A Systematic Review]. *Hu Li Za Zhi*. 2014 Dec;61(6):78-86. doi: 10.6224/JN.61.6.78. [Published in Chinese; English abstract in Pubmed 25464959]
- (7) Bashar, K et al (2014) **Role of Far Infrared Therapy in Dialysis Arterio-venous Fistula Maturation and Survival: Systematic Review and Meta-Analysis.** *PLoS ONE*.2014 Aug. 9(8): e104931.doi:101371/journal.pone.0104931

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