Concluding remarks on animal studies:

There has been showen that non tumorous tissue with impaired blood supply can be left in animals without causing serious adverse effects. Described changes in targeted tissue follow the same pattern in FD (Kopsky, Tumor devascularisation; Fortyn K., 1987, Morphology) and non FD oriented research (Thompson RL, 1908; Troell A.,1916; Sahin M , 2000; Griffiths J. , 1895; Awasum C A, 2008) and tumorous and non tumorous tissue. Arterial and venous occlusion is followed on the macroscopical level at first by swelling followed by shrinking and eventually by fibrous replacement of the tissue. Fibrous replacement has been confirmed on microscopical level as well. This process seems to be species independent at least in mammals and birds (Kopsky, 2010; Fortyn K., 1987; Thompson RL, 1908; Troell A.,1916; Sahin M , 2000; Griffiths J., 1895; Awasum C A, 2008).
Partial tissue fibrousis can be also caused by selective occlussion of lymph vessels as been demonstrated by Zhang in rat kidneys. (Zhang Taoyan, Disturbance) Fibrous replacement can be impaired by presence of collateral circulation as being proposed by Troell in the case of dog´s spleen. (Troell, 1916). There has been reported preservation of testicular tissue in dogs in some cases by Griffiths (Griffiths, 1895) and ovary in bitches reported by Awasum (Awasum, 2008)
It can be suppossed that reproductive tissue is more resistent to fibrous degeneration so there is especially needed complet occlussion of lymph and blood circulation which can be guaranteed by ligating hole tissue as been propossed by Morgan in the case of hens testes (Morgan, 1920) Probably the most interesting finding is the possibility of leaving ligated colon in situ even in the presence of bacterias in the lumen as being reported in pigs (Kopsky, 2010). Prompt transmural migration of endotoxine to system circulation from ligated colon was reported by Papa. Endotoxine enters system circulation as soon as 30 minut after colon devascularisation in dogs. (M.Papa, 1983) Proper examination of stoll can be therefore recommanded prior to any attempt of colon ligation.
There has been showen that ischemia injury of tumor tissue left in animal body do not cause serious adverse health impacts in studied animals (Kopsky, 2010; Fortyn K., 1987; Thompson RL, 1908; Troell A.,1916; Sahin M , 2000; Griffiths J., 1895; Awasum C A, 2008) and that products originated out of ischemia tumor tissue are capable to cause local cure of tumor (Kamijo, 2002) and even reduce number of distinct metastases in non FD connected research (Denekamp J, 1983).
Different effectivness between pig and rat model of FD animal model (Horak V., 2008) can be explained by differences in species immune systems or by different intrinsic tumor immonogenity since different types of tumors were used or by contribution of both of these factors.
Nevertheless HSPs induced immunity pathway seems to be of special importance in arrangement anti-cancer effect of FD in both of this animal models. Vitiligo is reported as an adverse effect in melanoma pig model (Horak V., 1999).
There is a possibility that not only melanomas but all melonocytes undergo some kind of genetic transformation in FD pig animal model and that activated immune systém do react to it. On the other hand induced autoimmune response can be an explanation too. There has been described cross reaction among melanoma cells and melanocytes in mice model. Melanomas reduction was induced by killing melanocytes in the presence of high level of HSP70. (Sanchez-Perez L, 2006)
These supports the importance of HSP pathway in FD but also indicates possibility of antigen cross activation in the same cell lines. The more over local vitiligo has been described in connected with the process of spontaneous melanoma regression supporting possibility of antigen cross activation in melanoma and melanocytes. (Papac JP. 1996) Changes in flow cytometry in FD treated and non treated MeLiM pigs do indicated possibility of change in Th polarity of immune response in favour to Th1. (Horak V., 2008).

Literature:

K. Fortyn, J. Hradecky, V. Hruban, V. Horak, P. Dvorak, J. Tichy. Morphollogy of regressive changes in the kidney following experimental ischaemia. Int Urol Nephrol. 1987; 19(1):9-19.

David Kopsky, MD., prof. dr. Jan M. Keppel Hesselink, MD, PhD, Remco Liebregts MD. Tumor devascularisation a compassionate use protocol. 2010, Pilot study of an immunological intervention of metastatic solid tumors

Thompson RL, Leighton WE. The Results of Chronic Parathyroiditis as obtained by Ligation of the Parathyroid

glandules in the Dog. J Med Res. 1908; 19(1):121-134.3.

20) Troell A. On ligation of splenic vessels as a substitute for splenectomy in blood diseases. Ann Surg. 1916 January; 63(1): 88–105

21) Sahin M, Tekin S, Aksoy F, Vatansev H, Seker M, Avunduk MC, Kartal A. The effects of splenic artery ligation in an experimental model of secondary hypersplenism., J R Coll Surg Edinb. 2000; 45: 148-52

22) Griffiths J. Effects upon the Testes of Ligature of the Spermatic Artery, Spermatic Veins, and of both Artery and Veins. J Anat Physiol. 1895; 30: 81–105.

23) Awasum C A, Hassan AZ, Remi-Adewumi BD, Achi CR, Ibrahim NDG, Raoul DK, Rafindadi RH. Neovascularisation of the ovary post ligation of ovarian vessels in bitches, Sokoto Journal of Veterinary Sciences 2008; 7:7-9

Morgan TH, The Effects of Ligating the Testes of Hen-Feathered Cocks. 1920, Biological Bulletin 1920; 39:248-256

Papa M, Halperin Z, Rubinstein E, Orenstein A, Gafin S, Adar R. The effect of ischemia of the dog's colon on transmural migration of bacteria and endotoxin. J Surg Res. 1983; 35:264-9.

Kamijo A, Koshino T, Uesugi M, Nitto H, Saito T. Inhibition of lung metastasis of osteosarcoma cell line POS-1 transplanted into mice by thigh ligation., Cancer Lett. 2002; 15; 213-9.

Denekamp J, Hill SA, Hobson B. Vascular occlusion and tumour cell death., Eur J Cancer Clin Oncol. 1983;19:271-5.

Horak V., Moravkova A., Strnadel J, Hradecky J, Usvald D, Vannucci L. Devitalization as a special surgical treatment inducing anti-cancer response – an experimental study in two animal models. CIMT cancer immunotherapy, 6th annual meeting; 2008 May 15-16; Mainz, Germany.

Horak V., Fortyn K., Hruban V., Klaudy J., Hereditary melanoblastoma in miniature pigs and its successful therapy by deviatization technique, Cell Mol Biol (Noisy-le-Grand) 1999; 45(7):1119-29.

Sanchez-Perez L, Kottke T, Daniels GA, Diaz RM, Thompson J, Pulido J, Melcher A, Vile RG. Killing of normal melanocytes, combined with heat shock protein 70 and CD40L expression, cures large established melanomas.J Immunol. 2006; 177:4168-77.

Papac JP. Spontaneous regression of cancer. Cancer Treat Rev 1996; 22: 395-423