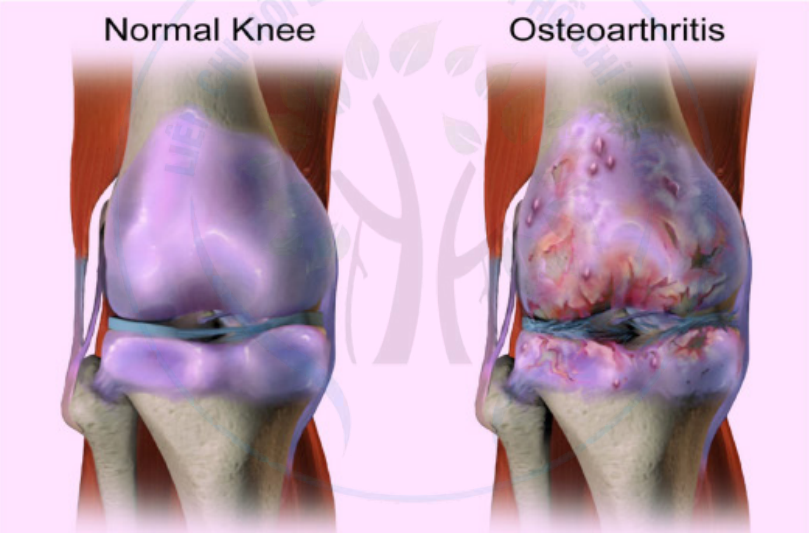
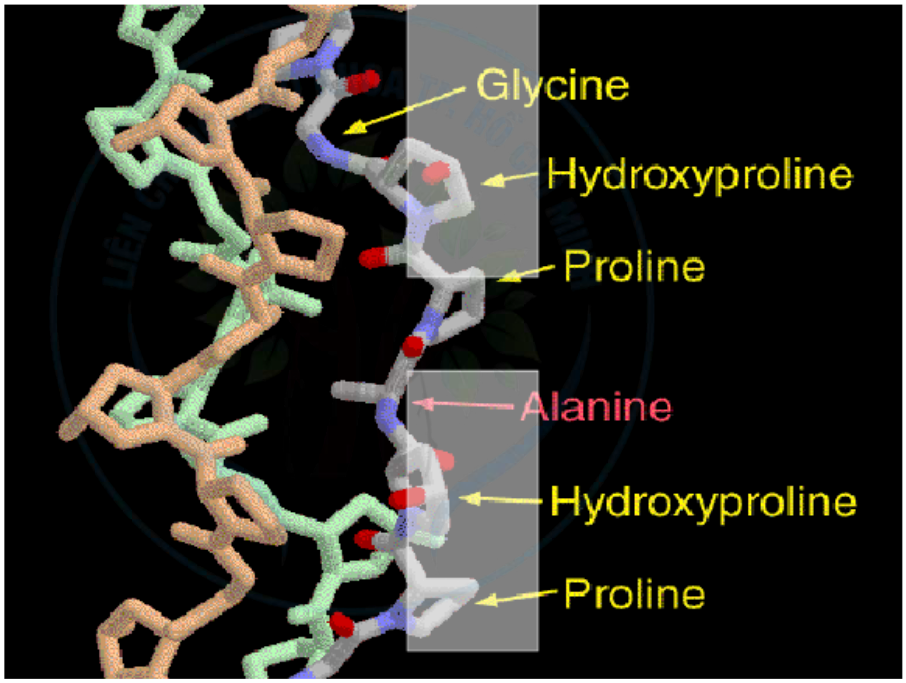
Intra-articular joint injection of bioactive collagen peptides for knee OA

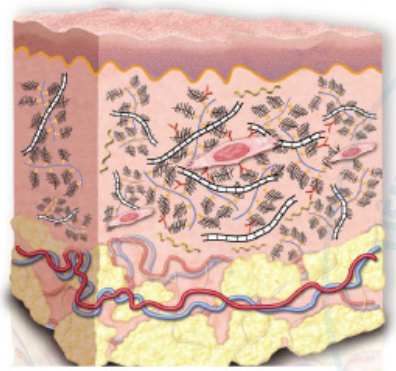


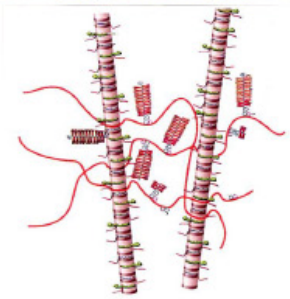
Prof. Ph.M.D. Benedetto Pinto

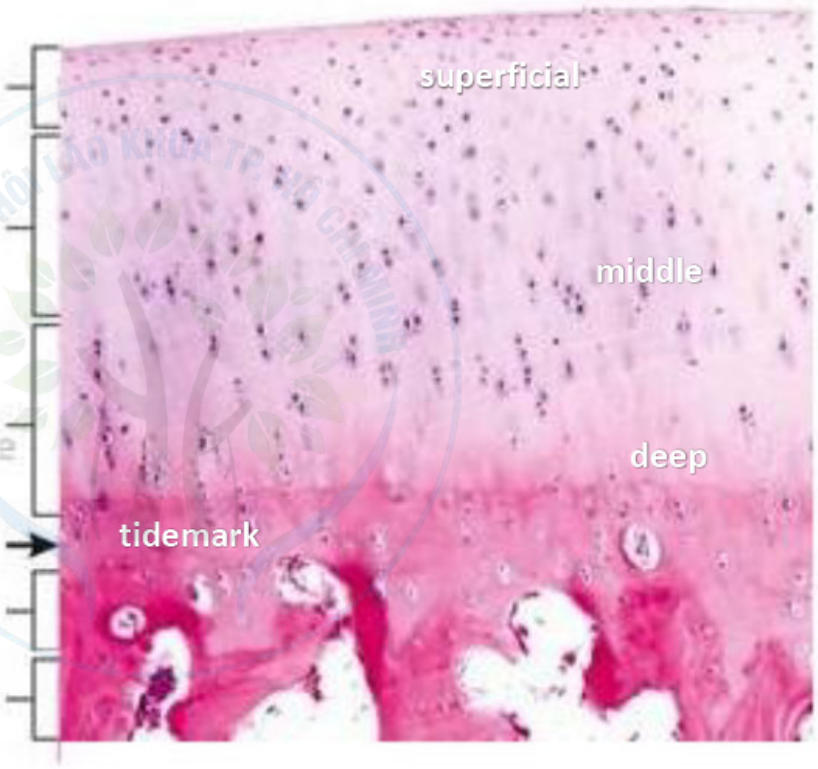
collagen peptides

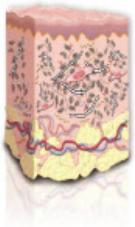


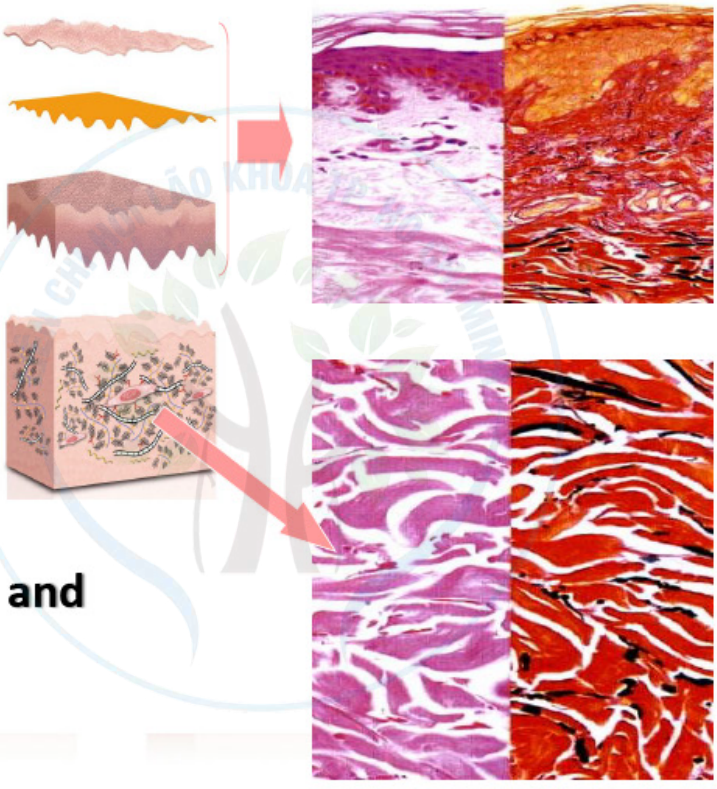
cartilage





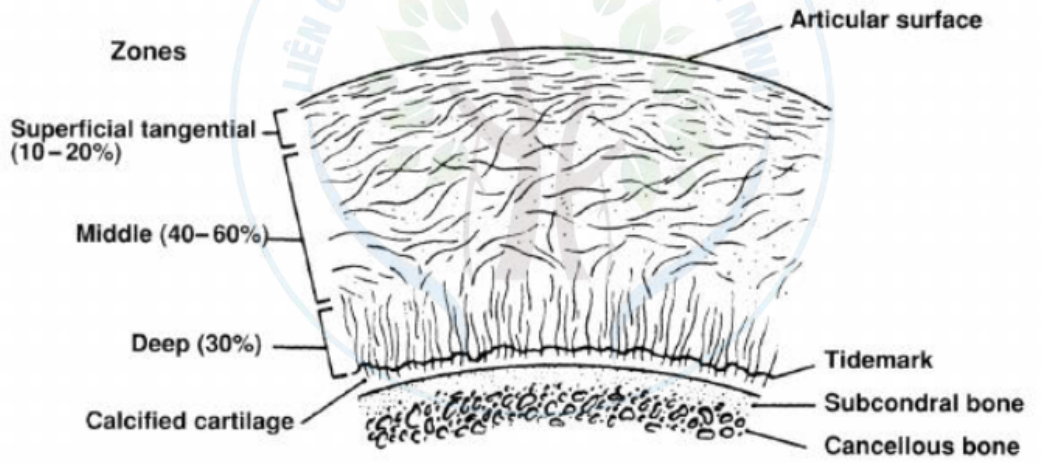






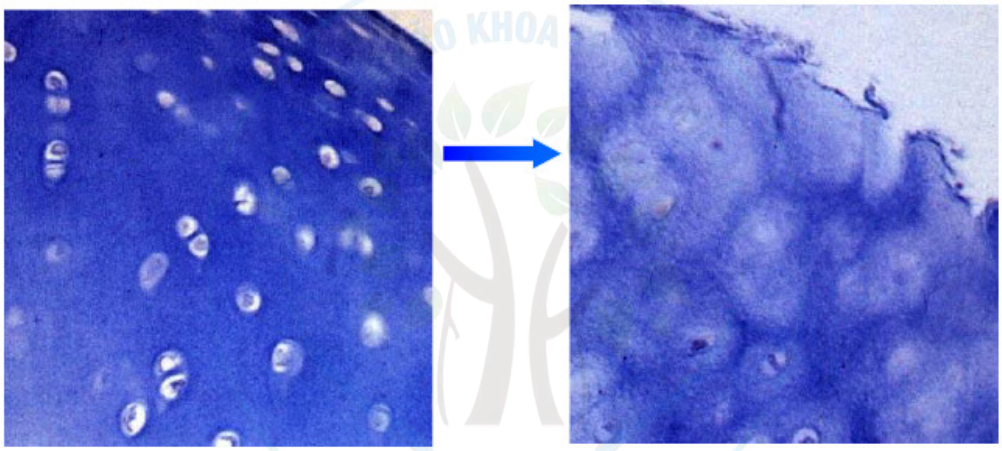
different layers and orientation of collagen fibers

the proteoglycan gel (giving a baseline isotropic diffusivity) and the highly anisotropic collagenous fibre network.

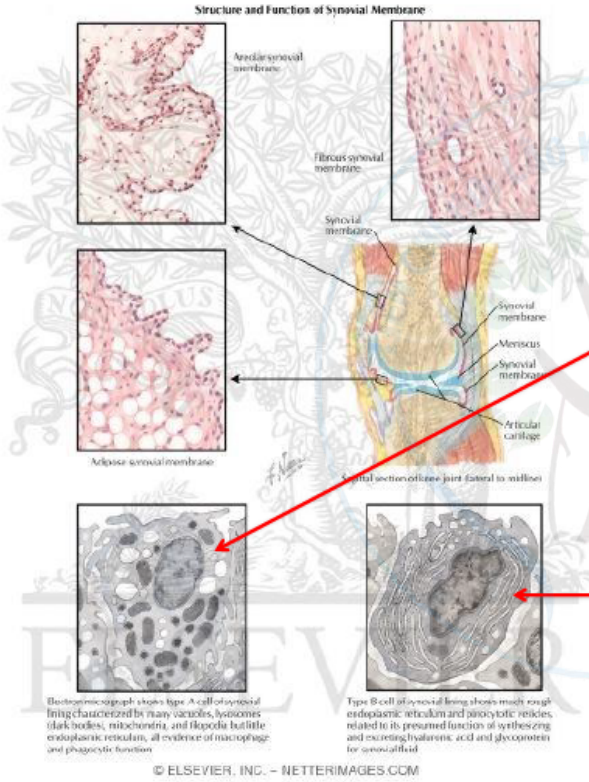


normal

arthrosis



The cell population of the cartilage is the 2-3% of the whole tissue



In the synovial tissue there are two types of cells.

- Type A: clean the joint from debris
- Type B: produce the synovial fluid to keep the cartilage healthy.

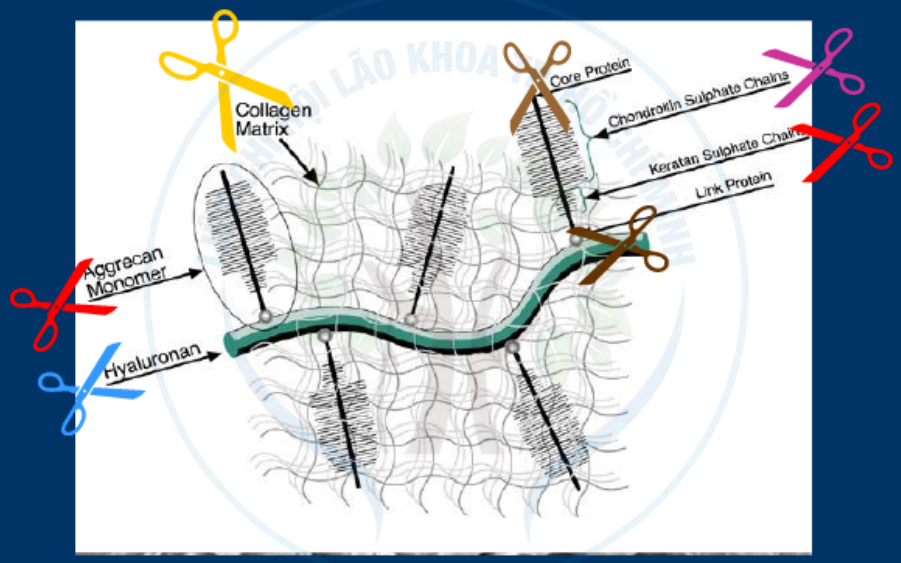
synovial fluid

- The synovial fluid lubricates the articulating joints and reduces friction.
- As the synovial fluid acts as a dilatant fluid, it possesses rheopectic properties. Synovial fluid has a more vicious capacity when the pressure is applied. The synovial fluid present in diarthrotic joints will become thick the moment shear in order to protect the joint and subsequently. Normal viscosity of the synovial fluid instantaneously resumes its lubricating function between shocks.
- Synovial fluid usually supplies oxygen and nutrients, further they remove carbon dioxide and metabolic waste from the chondrocytes present in the surrounding cartilage tissues.
- The pressure acts on the joints forces to secrete hyaluronan in the fluid, that acts on the synovial membrane, which acts as a barrier against cells and helps to migrate into or out through the joint space. The molecular sieving is completely dependent on the molecular weight of the hyaluronan.
- Hyluronan play the main function in the synovial fluid . Thanks to its hydrophilic properties protect the cartilage tissue.

metabolism

20 days

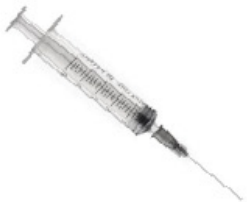
proteoglic
an
Ha

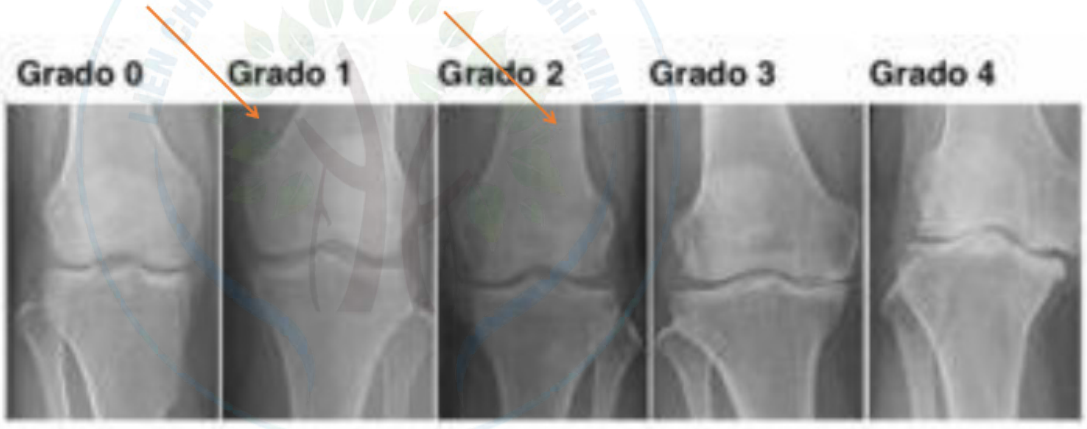


3 years

collagen

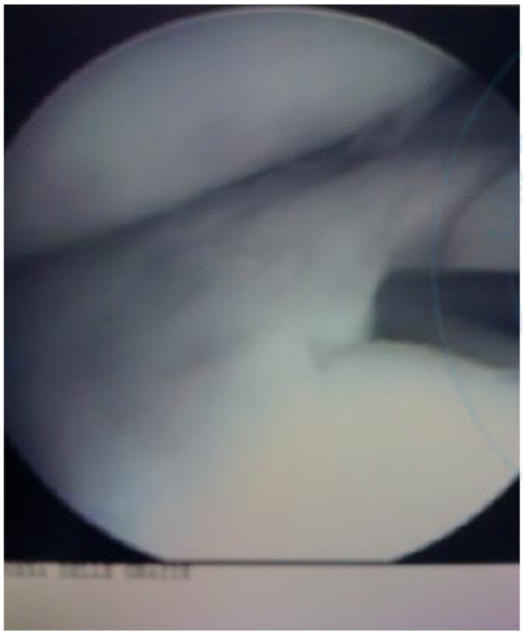
when to inject collagen peptides

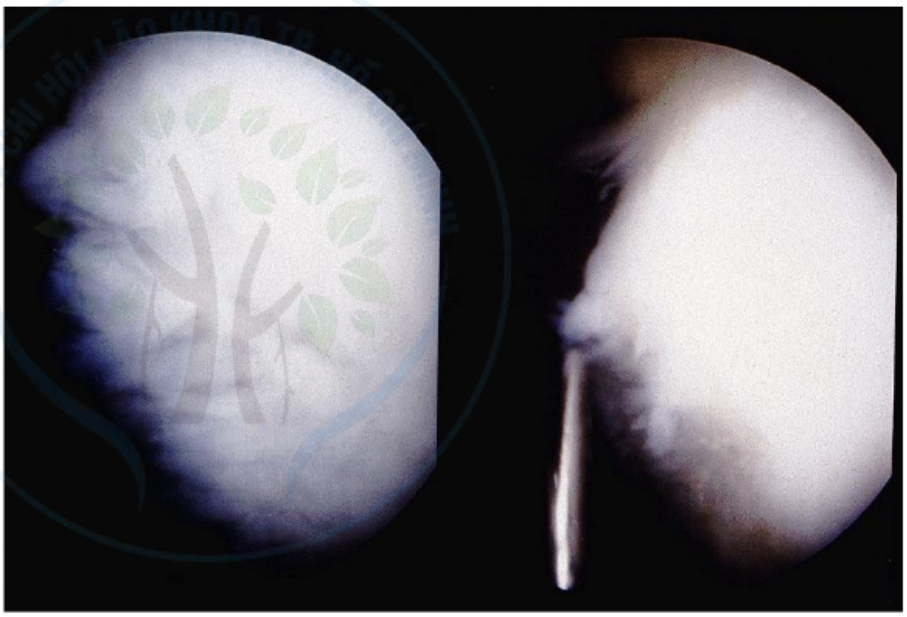




kellgren-Lawrence class.

conservative treatment





What news about collagen peptides

- J. Clin. Med. 2019, 8, 975; doi:10.3390/jcm8070975 www.mdpi.com/journal/jcm ***Article Intra-Articular Injection of Hydrolyzed Collagen to Treat Symptoms of Knee Osteoarthritis. A Functional In Vitro Investigation and a Pilot Retrospective Clinical Study***
- Paola De Luca 1,†, Alessandra Colombini 1,†, Giulia Carimati 2, Michelangelo Beggio 3, Laura de Girolamo 1,* and Piero Volpi 2

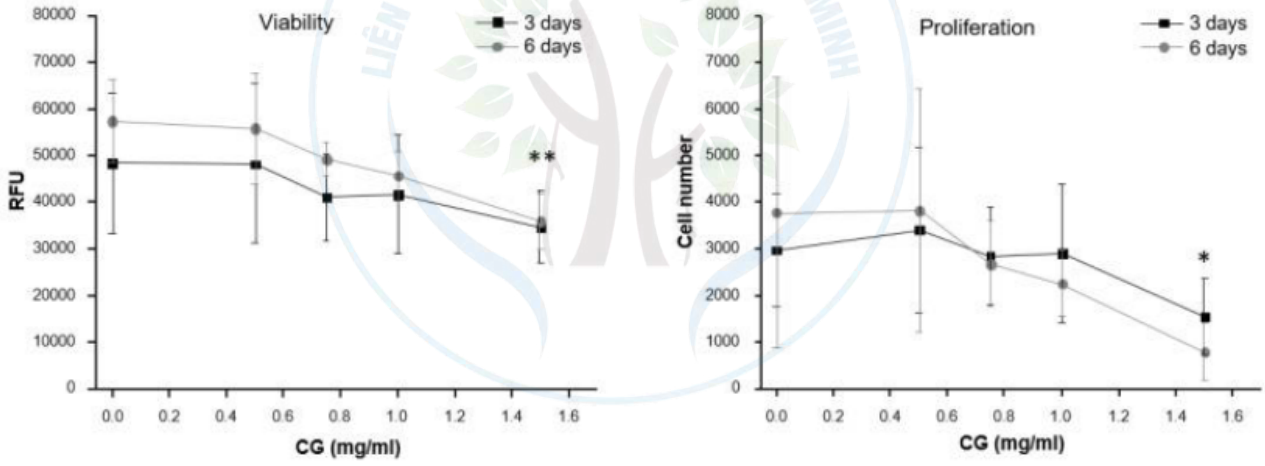
Conclusions Results of the present study show that CG may prompt chondrocytes to produce hyaline cartilage and counterbalance the normal reparative response that would lead, instead, to fibrous tissue formation. They also indicate CG may be a safe and effective adjuvant in the treatment of symptomatic knee OA by intra-articular injection. The overall results are extremely promising and highlight the need for further controlled prospective studies to investigate the full extent of the beneficial effects of CG treatment and whether intra-articular CG injection may be more beneficial than other non-pharmacological treatments already available in the clinical practice

- ***Long-Term Effectiveness of Polymerized-Type I Collagen Intra-Articular Injections in Patients with Symptomatic Knee Osteoarthritis: Clinical and Radiographic Evaluation in a Cohort Study***
- Adrián Borja-Flores,1Salvador I. Macías-Hernández
- ,2Gabriela Hernández-Molina 3Andric Perez-Ortiz,4Eloy Reyes-Martínez,1José Belzazar-Castillo de la Torre,1Laura Ávila-Jiménez,5María Cristina Vázquez-Bello,5Marco Antonio León-Mazón,6Janette Furuzawa-Carballeda,3Gonzalo Torres-Villalobos,7and Fernanda Romero-Hernández7 et al

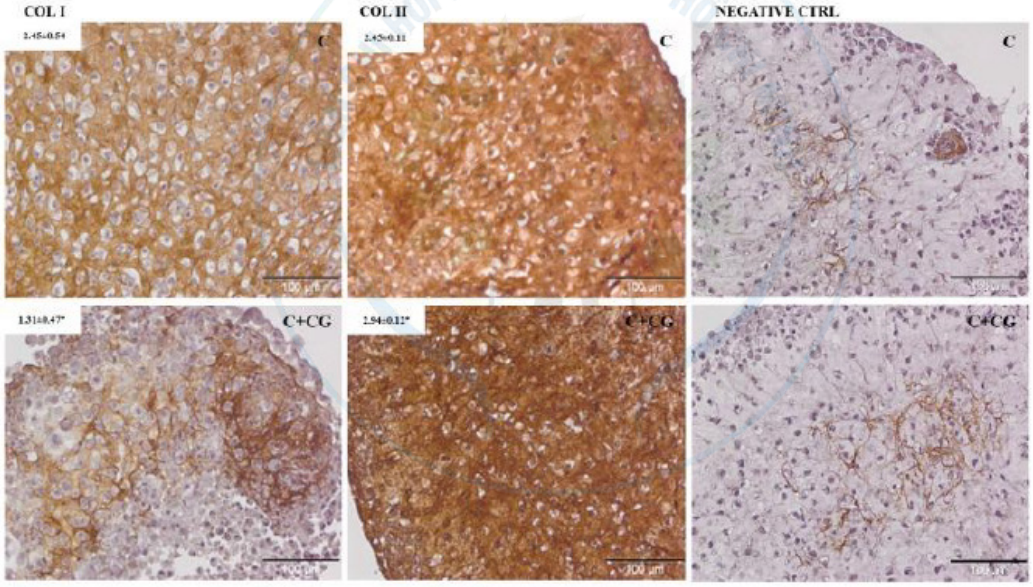
Conclusion

Polymerized-type I collagen has an excellent long-term clinical outcome and a safe profile. The obtained data show that polymerized-type I collagen improves functional disability, decreases pain, and increases the time of surgical deferral of TKR, suggesting that it could slow or halt the radiographic evolution of the disease. It is a nonsurgical treatment option that certainly deserves future research

A significant difference with control (no CG) was observed only when the higher concentration (1.5 mg/mL) was used for 6 days ($p < 0.01$ for viability and $p < 0.05$ for proliferation). No significant difference was observed between values at 3 and 6 days at any CG concentration. As CG 1.5 mg/mL was observed to affect viability and proliferation, all the following experiments were carried out using CG 1 mg/mL



When cells were cultured in a chondrogenic medium, they produced both type-I and type-II collagen, whereas when CG was added, high deposition of type-II collagen and inhibition of type-I collagen deposition were observed



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0270-7306/84/061163-06$02.00/0
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Location of 64K Collagen Producer Chondrocytes in Developing Chicken Embryo Tibiae

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Received 14 November 1983/Accepted 23 March 1984

The synthesis of a new low-molecular-weight collagen by cultured chicken embryo chondrocytes has been recently demonstrated (Capasso et al., Exp. Cell Res. 142:197–206, 1982; Gibson et al., J. Cell Biol. 93:767–774, 1982; Schmid and Conrad, J. Biol. Chem. 257:12444–12450, 1982). In this paper we report results on the location of chondrocytes synthesizing this new collagen (64K collagen) in the developing chicken embryo. The 64K collagen is synthesized in very large amounts by cells concentrated at the diaphysis of 9-day-old and at the epiphysis of 17-day-old embryo tibiae. These regions are characterized by a remodeling of the cartilage matrix leading to the replacement of the cartilage with bone tissue; therefore, this collagen appears to be a marker of a specific developmental stage of chondrocytes. The origin of cells competent for the synthesis of the 64K collagen is also discussed.

Organogenesis of the tibia begins with the condensation into limb buds of mesenchymal cells and their subsequent differentiation into chondrocytes. A marker of this event is the transition from type I to type II collagen synthesis and the deposition of this specific cartilage collagen in the extracellular matrix (13). The ossification process involves some modifications of the chondrocyte morphology and a deep rearrangement of the extracellular matrix, including its calcification. At later stages of development the cartilage tissue is progressively replaced by bone tissue and bone marrow (1).

Recently it has been shown that chicken embryo chondrocytes synthesize in culture, in addition to the major type II collagen, some low-molecular-weight collagenous proteins (4–6, 10). One of these proteins, named in our laboratory 64K collagen on the basis of its apparent molecular weight (6), is made in relatively high amounts by tibial chondrocytes from 17-day-old embryos. This collagen appears to be a specific product of the cartilage cells, and its synthesis is blocked, as for the other differentiation products, after Rous sarcoma virus transformation (7). When correctly hydroxylated, the 64K collagen is deposited in the extracellular matrix both in vitro and in vivo (4a). The 64K collagen has an amino acid composition comparable to that reported for the SC collagen (12; N. Quarto, B. Cancedda, and F. Denzadi-Cancedda, manuscript in preparation) and properties very similar to those of the G and SC collagens described by other groups (6, 12); it therefore must be considered identical to those collagens.

In standard culture conditions, only chondrocytes derived from tibiae synthesize this protein in large amounts (4, 10, 11). A possible relationship between the developmental stages of tibiae and the capacity of derived chondrocytes to synthesize the 64K collagen has not been yet carefully investigated. This collagen is synthesized by cultures of chondrocytes both from specific regions of 12-day-old embryo tibiae (11) and from whole tibiae of 17- to 19-day-old embryos (4). No data are available for chondrocytes derived from tibiae at earlier stages of development.

In chondrocytes derived from sterna, a significant synthesis of this collagen has been demonstrated only when the cells were grown in tridimensional collagen gels (6), suggesting that the cell environment could affect the expression of this protein.

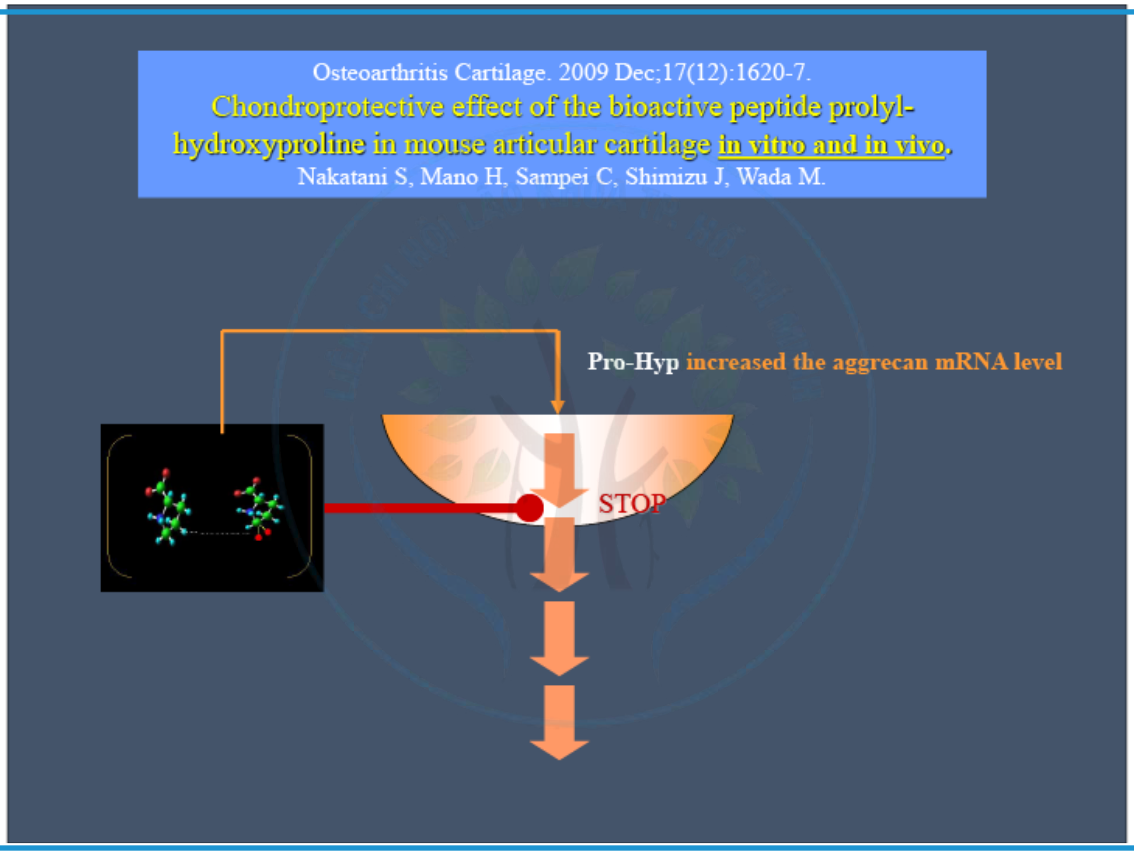
In this paper we report some studies on the localization in different tibia regions and the timing of appearance of the 64K collagen during chicken embryogenesis. The possible origin of chondrocytes competent for the synthesis of this collagen is also discussed.

MATERIALS AND METHODS

Cell sources. Whole tibiae from embryos at different stages of development (see below) were digested with, per ml, 70 U of collagenase I (Worthington), 100 U of collagenase II (Worthington), 0.75 mg of trypsin (Difco), and 2% chicken serum for 30 min at 37°C to remove tissue debris and perichondrium. The tibiae were separated from the tarsus, cut into slices under a microscope, and digested a second time with the same mixture. To obtain a complete dissociation of the cartilage tissues into single cells, the timing of the digestion was increased according to the age of embryos, from 45 min for 8-day-old embryos to 2 h + 1 h for 17-day-old embryos. When indicated, slices from five different regions of tibiae (distal epiphysis, intermediate [metaphysis], diaphysis, intermediate [metaphysis], and proximal epiphysis; see also Fig. 2 and Table 1) were digested separately. For day 9 embryos the epiphysis and the adjacent metaphysis segment were combined. The histological characteristics of each region were analyzed by histochemical staining (see below).

[^{35}S]methionine labeling of the cells. Cells obtained by the digestion of the cartilage tissues were plated at 5×10^5 cells per 3.5-cm^2 dish in F12 medium with fetal calf serum. After 16 h the cells were first starved for methionine for 2 h in F12 medium lacking methionine and supplemented with 2% dialyzed fetal calf serum plus 50 μg of ascorbic acid per ml; the cells were then incubated with 20 μCi of [^{35}S]methionine (Amersham; per ml in the same medium). Cell layers were washed twice with phosphate-buffered saline and lysed in 50 mM Tris-hydrochloride (pH 7.4)–100 mM NaCl–1 mM EDTA–0.5% sodium dodecyl sulfate (SDS) (TNE-SDS buffer). In some experiments cells were also labeled 4 and 8 days after plating, without major differences in the results obtained.

* Corresponding author.



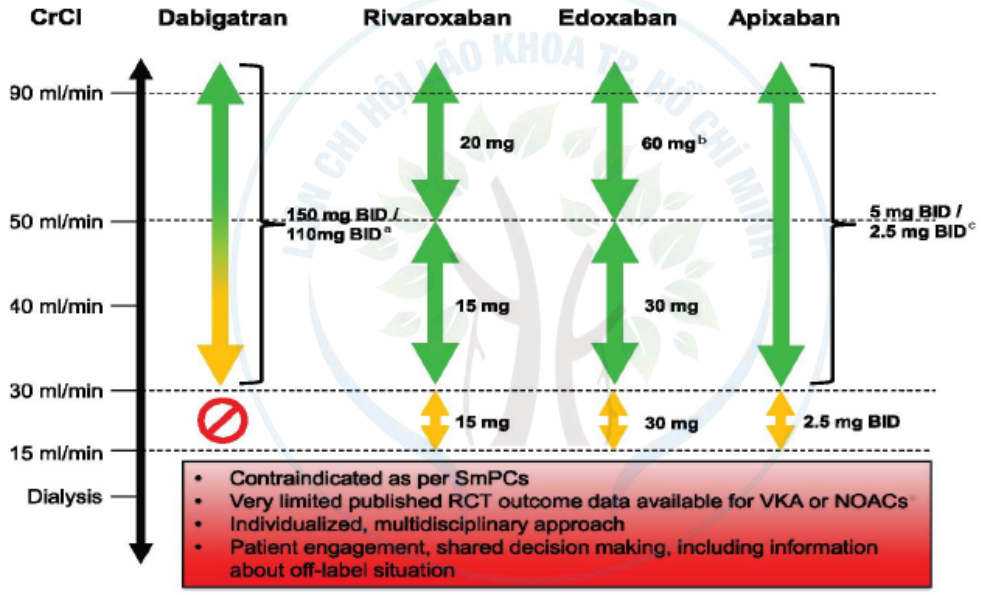
why collagen peptides

- 1) collagen is the main component of the ECM
- 2) collagen incorporates within it HA and proteoglicans
- 3) collagen change polarity according to the mechanical stress
- 4) collagen differentiate mesenchimal cell and stem cell to condhocytes
- 5) collagen transfers information to the chondrocytes thanks to integrin connections
- 6) collagen boost cell prloferation
- 7) scaffold for cartilage regeneration are made by collagen


WWW.JPERGRAFANDO.IT
thanks

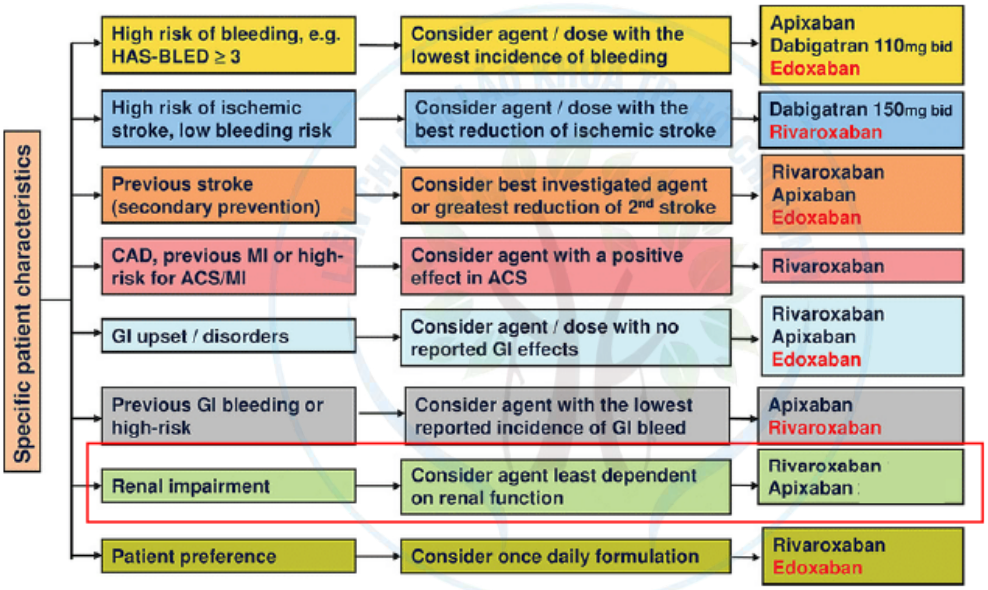
Lựa chọn NOAC trên bệnh nhân suy thận – EHRA 2021

EHRA European Heart Rhythm Association
European Society of Cardiology



Jan Steffel, Ronan Collins, Matthias Antz, Pieter Cornu, Lien Desteghe, Karl Georg Haeusler, Jonas Oldgren, Holger Reinecke, Vanessa Roldan-Schilling, Nigel Rowell, Peter Sinnaeve, Thomas Vanassche, Tatjana Potpara, A John Camm, Hein Heidbüchel, External reviewers, 2021 European Heart Rhythm Association Practical Guide on the Use of Non-Vitamin K Antagonist Oral Anticoagulants in Patients with Atrial Fibrillation, *EP Europace*, Volume 23, Issue 10, October 2021, Pages 1612–1676,

Lựa chọn NOAC trên bệnh nhân suy thận



Okumura, Ken et al. "Special considerations for therapeutic choice of non-vitamin K antagonist oral anticoagulants for Japanese patients with nonvalvular atrial fibrillation." *Clinical cardiology* vol. 40,2 (2017): 126-131. doi:10.1002/clc.22596

Lựa chọn NOAC trên bệnh nhân suy thận

Subjects with nonvalvular atrial fibrillation and CrCl between 15 and 49 ml/min

First choice	Apixaban 5 mg twice daily (or 2.5 mg twice daily in presence of one or more additional criteria: age ≥ 80 years, body weight ≤ 60 kg, serum creatinine ≥ 1.5 mg/dl)
	Rivaroxaban 15 mg once daily → Liều đơn giản, ngày 1 lần, không phải chỉnh liều theo tuổi và cân nặng
	Edoxaban 30 mg once daily
Second choice	Dabigatran 110 mg twice daily
Not recommended	Dabigatran 150 mg twice daily
	Rivaroxaban 20 mg once daily
	Edoxaban 60 mg once daily

Di Lullo L, Ronco C, Cozzolino M, et al. Nonvitamin K-dependent oral anticoagulants (NOACs) in chronic kidney disease patients with atrial fibrillation. *Thromb Res.* 2017;155:38-47. doi:10.1016/j.thromres.2017.04.027

Kết luận

- Suy thận làm gia tăng nguy cơ đột quỵ, biến cố tim mạch và nguy cơ xuất huyết ở bệnh nhân rung nhĩ
- NOAC ưu thế hơn warfarin về an toàn, hiệu quả và ít làm suy giảm chức năng thận hơn warfarin
  - Rivaroxban: hiệu quả dự phòng đột quỵ và độ an toàn trên nhóm bệnh nhân rung nhĩ kèm suy thận được chứng minh từ RCT đến thực tế lâm sàng.
  - Rivaroxaban: bảo tồn chức năng thận, giảm các biến cố trên thận so với VKA
- Các khuyến cáo và đồng thuận: rivaroxaban 15 mg một trong những lựa chọn đầu tay trên nhóm bệnh nhân rung nhĩ kèm suy thận.