SERVIZIO SANITARIO REGIONALE
EMILIA-ROMAGNA
Istituti Ortopedici Rizzoli di Bologna

San Michele in Bosco
Area Monumentale I.R.C.C.

Autogenous mesenchymal stem cells as adiuvant to healing in congenital pseudoatrhrosis surgical treatment of type 1 neurofibromatosis in children

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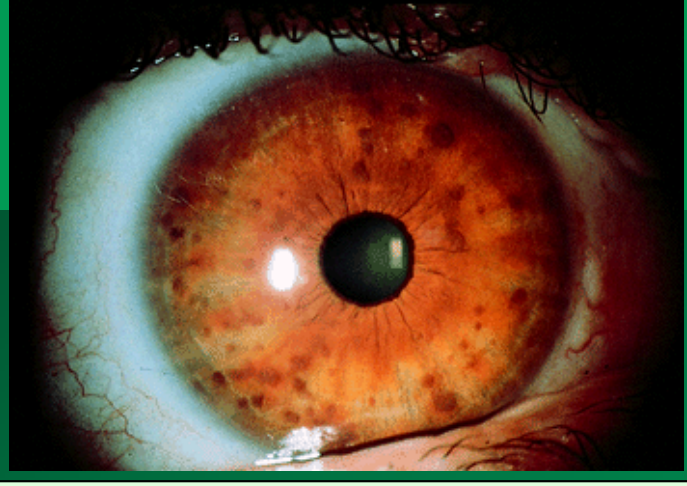
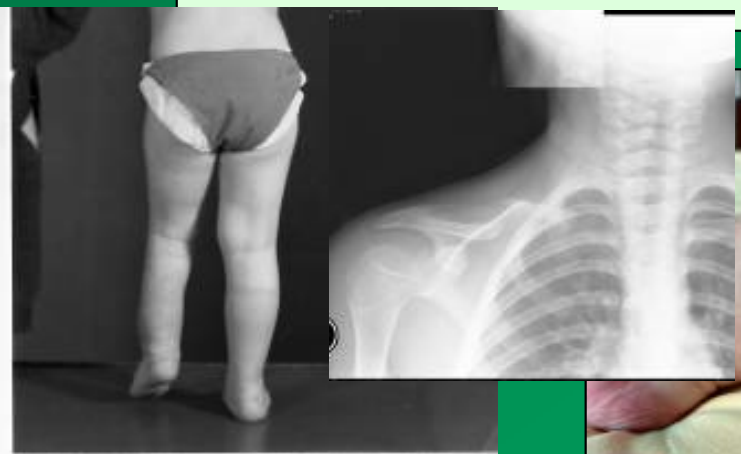


The Type 1 neurofibromatosis is a multisystem disease trasmitted by autosomal dominant inheritance, incidence is 1/2500 and 1/3000 and prevalence is 1/5000.

The expression is variable and the diagnosis is fonded on the presence of two of these signs

- >6 caffe'-au-lait spots
-Two skin neurofibromin
-Lisch nodles
-Optical nerve glioma
-Bone dysplasia (tibial, clavicola)



The long bone dysplasia is most frequent in the tibial bone and presents spontaneous fractures that do not consolidate. This is one of the most challenging condictions in pediatric orthopaedics because of the very poor life's quality of affected patients

Infact they develop a progressive lower limb's discrepancy
And need particular shoes and plasters

Actually therapeutic options in the treatment of the tibial congenital non union include different possibilities according to the severity and location of lesions and also the patient's age.

The usual treatment of tibial non union is characterized by repeated surgical procedures (intramedullary nailing or external fixator) which often fail with poor outcome, severe disability and sometimes amputation

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Intramedullary nailing

Bone graft and intramedullar nail
Dobbs MB (JBJS Am 2004, JBJS AM 2005)
16 pz on 21 they have shown turns out to you satisfactory.
5 pz subordinates to amputation.
12 riefractures/10 ankle valgus /11 leg discrepancy (WAS medium 14 years).

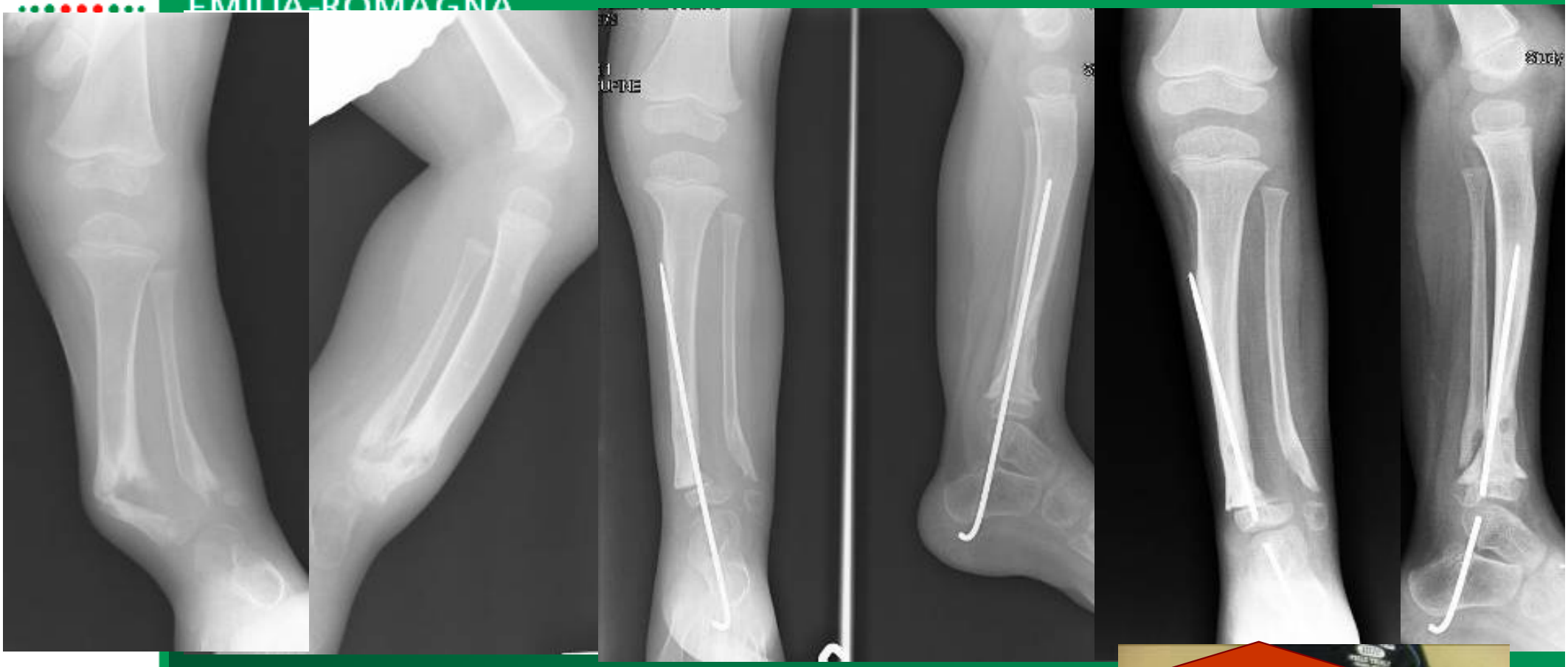
Jonsthon CE (JBJS Am 2002) BONY GRAFT AND INFIBULO: in 11 pz on 23 result of consolidation of the non union without reinterventi and can give complete weight bearing, important axial shunting lines (WAS NOT 4-14 years). It is necessary to act also on the fibula.

Kim HW (Clin Orthop Relat Res 2002) BONY GRAFT AND INFIBULO: 4 pz on 11 they have had consolidation after the participation. 4 pz numerous ulterior participations. 2 pz they have endured amputation. Fatttori prognostici denied to you if the focolaio it is tos be distant them and if also the fibula is affection.

External fixator

USE OF EXTERNAL FIXATOR (ILIZAROV)

- Cho TJ (JBJS Br 2008) ILIZAROV: 43 cases in 23 pz. Rate rifrattura to 5 years of 47% nearly always in the same center. Risk increased if osteosintesi carried out under the 4 years and if present pseudoarthrosis also in the fibula. Important to stabilize also the fibula.



Surgical procedure often fails

Loss of position of the nail

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Recently new strategies based on the use of autogenous mesenchymal stem cells (MSC) have been proposed. MSC pool contains precursors of osteogenic differentiation, that may enhance bone repair and regeneration .

Recent studies demonstrated that MSC generated from iliac crest are more osteogenic than those generated from the affected tibia.

The bone Microenvironment does not influence their osteogenic potential

SC Laboratorio
di Fisiopatologia
Degli
npianti Ortopedici

1. Magnani M, Lampasi M, Granchi D, Devescovi V, Donzelli O. USE OF STEM CELLS IN SURGICAL TREATMENT OF CONGENITAL PSEUDARTHROSIS IN CHILDREN. Transaction of 16th Annual Meeting of European Orthopaedic Research Society, Bologna 7-9 June 2006, Abstract P14.
2. Devescovi, Pagani S, Amato I, Magnani M, Donzelli O, Ciapetti G, Giunti A, Baldini N, Granchi D. OSTEOGENIC POTENTIAL OF BONE MARROW MESENCHYMAL STEM CELLS IN CONGENITAL TIBIAL PSEUDARTHROSIS ASSOCIATED WITH TYPE 1 NEUROFIBROMATOSIS. Transaction of 16th Annual Meeting of European Orthopaedic Research Society, Bologna 7-9 June 2006, Abstract P168.
3. DeVescovi V, Pagani S, Amato I, Ciapetti G, Donzelli O, Magnani M, Baldini N, Granchi D. BIOLOGICAL BASIS FOR THE USE OF MESENCHYMAL STEM CELLS IN THE TREATMENT OF TIBIAL CONGENITAL PSEUDARTHROSIS ASSOCIATED WITH TYPE 1 NEUROFIBROMATOSIS. International Conference on Advances in Biomaterials for Drug Delivery and Regenerative Medicine, Capri June 11-16, 2006. Abstract OC45, pag. 87.

Granchi D. DeVescovi V, Leonardi E, Baglio SR, Donzelli O, Magnani M, Baldini N, MESENCHYMAL STEM CELLS FOR THE TREATMENT OF TIBIAL CONGENITAL PSEUDARTHROSIS ASSOCIATED WITH TYPE 1 NEUROFIBROMATOSIS. Workshop Rare Disease and Orphan Drugs. Istituto Superiore di Sanità, Rome, Novembre 7-8, 2007. Abstract pag. 57.

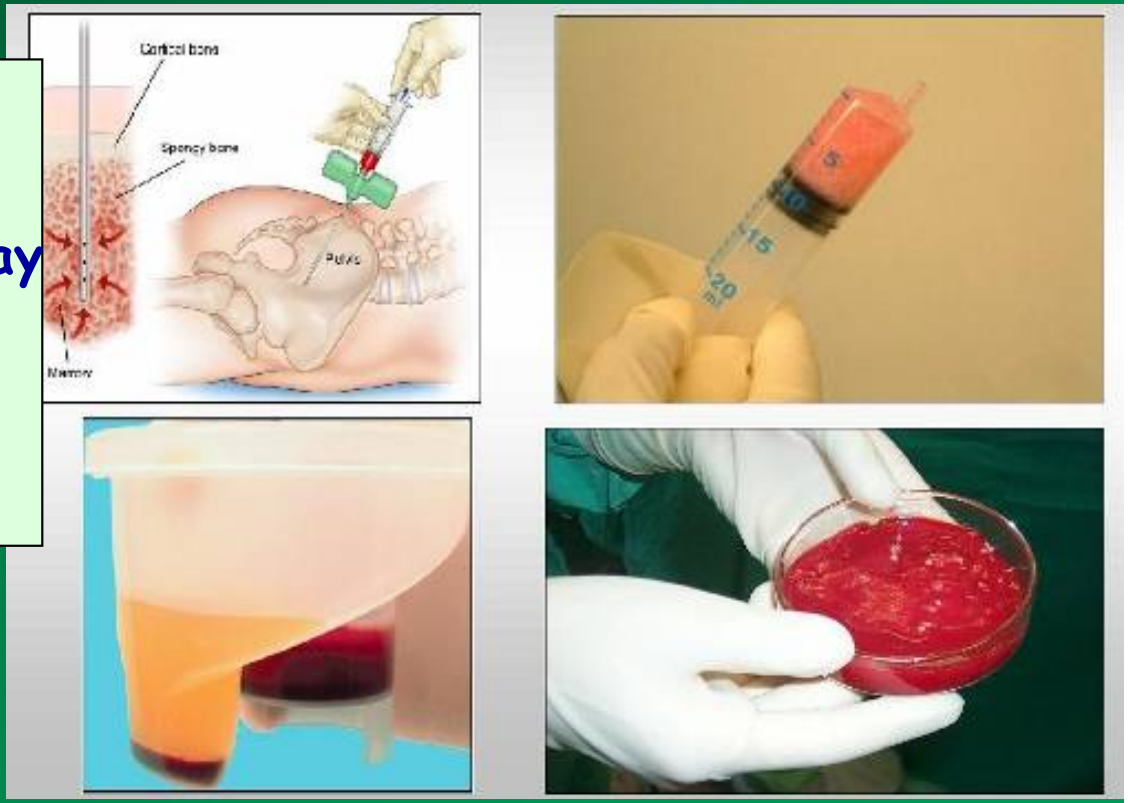
DeVescovi V, Leonardi E, Baglìo SR, Donzelli O, Magnani M, Baldini N, Granchi D. Giunti A. STUDY OF MARROW STROMAL CELLS OSTEOGENIC POTENTIAL FOR THE TREATMENT OF TIBIAL CONGENITAL PSEUDARTHROSIS ASSOCIATED WITH TYPE 1 NEUROFIBROMATOSIS. X Congresso Nazionale della Società Italiana di Ricerche in Ortopedia e Traumatologia (IORS) 2008, Messina 12-13 settembre 2008. Abstract, pag. 66.

6. Granchi D. DeVescovi V, Leonardi E, Baglio SR, Donzelli O, Magnani M, Baldini N, MESENCHYMAL STEM CELLS FOR THE TREATMENT OF TIBIAL CONGENITAL PSEUDARTHROSIS ASSOCIATED WITH TYPE 1 NEUROFIBROMATOSIS. Workshop Rare Disease and Orphan Drugs. Istituto Superiore di Sanità, Rome, October 29-31, 2008. Abstract pag. 71.

Full paper in preparazione:
Granchi D. DeVescovi V, Baglio SR, Donzelli O, Magnani M, Giunti A Baldini N. OSTEOGENIC DIFFERENTIATION OF BONE MARROW STROMAL CELLS IN PATIENTS AFFECTED BY CONGENITAL PSEUDARTHROSIS OF THE TIBIA.

The first surgical step is Bone marrow's aspiration from the iliac crest by an anterior or posterior approach in general anaesthesia.
(we collect 60-100 ml according to the patient's age and weight)

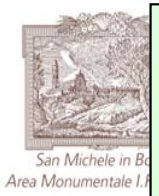
We add also autogenous platelet's grow factors (PFR), obtained one day before surgery from the patient's Venous blood



The second step is the curettage of the non union site, followed by surgical stabilization using an external circular fixator according to Ilizarov technique or an intramedullary nail.
(according to the **Charnlay**-Williams procedure).
Finally we put in the bone gap a mix of: packed of lyophilized bone graft,autologous stromal cells and growth factors and
After we cover it with a periostal flap

First results show a bone healing in 90/180 days.

Next goal: use autologous stem cells obtained from the bone marrow, select and expand them in vitro then, after 30 days, implant them during the surgical stabilisation



Many problems must still be resolved to use in the future concentrated mesenchimal stem cells and in vitro expanded

still long road

thanks

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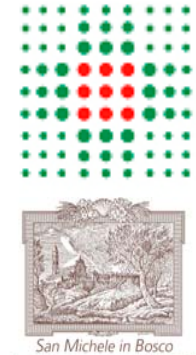

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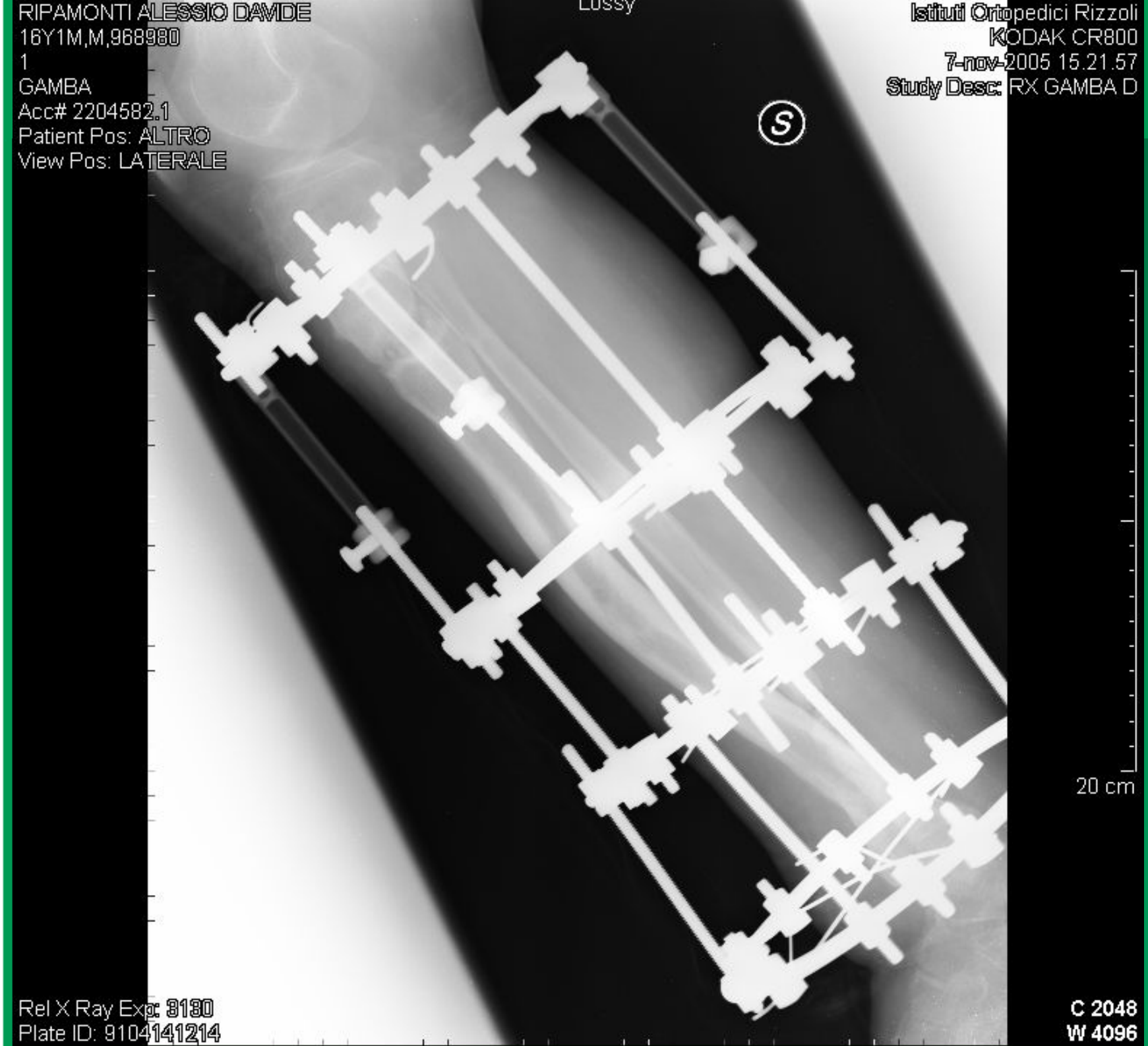

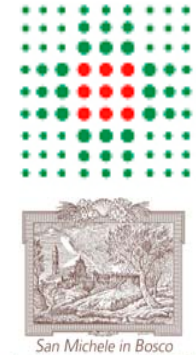

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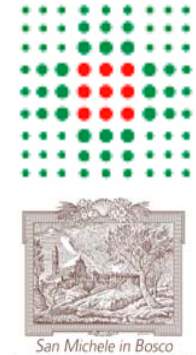

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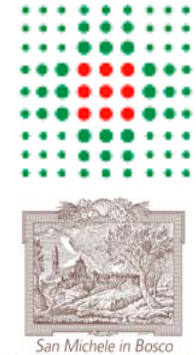

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