



## An Innovative Way to Create and Treat the Purulent Liver Abscess in a Surgical Experiment

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**Received:** April 12, 2021

**Published:** June 23, 2021

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### Abstract

**Relevance:** The development of new methods for creating liver abscesses will allow us to clarify diagnostic standards and justify new minimally invasive methods of surgical intervention and postoperative therapy. The aim is to experimentally substantiate an innovative method for creating a HAP and the effectiveness of the combined use of low-intensity laser radiation (LLI) and metal nanocomplex (NC) in the surgical treatment of liver abscesses. Material and methods. The creation of a liver abscess was carried out in an experiment on 80 laboratory rabbits. In a certain proportion of the liver under the control of ultrasound for 5 days was carried out with an infected modified catheter with a silicone rubber balloon at the distal end, where a polystam of staphylococcus and *Escherichia coli* was used as the causative agent of the pathological process, while a delimited gap cavity was formed.

**Treatment:** PLA was performed for 14 days, and the animals were divided into 4 groups of 20 in each. The animals of the first group were sanitized with furacilin and the cavity the use of antibiotics. Animals of the second group underwent cavity and NILI sanitation. Animals of the third group underwent cavity sanitation using a 0.24% solution of intralipid containing NK. Animals of the fourth group underwent sanitation of the abscess cavity in combination with the introduction of NK and the use of NILI. Clinical, planimetric, microbiological, morphological, and instrumental methods were used to confirm the simulated abscess.

**Results and Discussion:** Performing a transcutaneous puncture of the liver with laser support provides reliable cholestasis and hemostasis using an infected two-channel catheter with a balloon guarantees the formation of a GAP with the specified characteristics in a short time. Combined use of NC and NILI provides purification from the pathogen of the PLA cavity by the 7<sup>th</sup> day of treatment and complete obliteration of the abscess cavity by the 20<sup>th</sup> day of treatment.

**Keywords:** Purulent Liver Abscess (PLA); Metal Nanocomplex (NC); Low-intensity Laser Irradiation (LLI)

### Introduction

The frequency of purulent-inflammatory complications in liver diseases reaches 8.7 - 12.8% [1-3]. Significantly improve the results of surgical treatment of purulent liver abscesses (HAP) allowed the introduction of ultrasound, computer and magnetic resonance imaging [4,5], in addition, the use of these studies can

contribute to the development of new methods of modeling and treatment of HAP [7,8].

In the literature, several methods of treating HAP are known: surgical rehabilitation of a purulent focus, conducting antibacterial, anti-inflammatory, desensitizing therapy [9,10]. Currently, the effect of local continuous intra-arterial antibacterial therapy on

the postoperative period in patients with liver abscesses, as well as the method of puncture-drainage treatment of abscesses under the control of ultrasound, has been proven [11]. However, the use of these methods of treatment in venom cases does not allow to conduct a qualitative assessment. treatment of the abscess cavity due to the ineffective local action of drugs [12]. Today, there are reports about the antimicrobial effectiveness of metal nanoparticles, in particular copper nanoparticles at a concentration of 1 mg/ml [13]. At the same time, the introduction of nanoparticles into the wound stimulates the mechanisms of regulation of the trace element composition and the activity of antioxidant enzymes. Besides, there is a wound-healing effect, which is especially important in the treatment of infections caused by strains resistant to currently used antibiotics [14,15].

Currently, the effectiveness of laser technologies in the treatment of PLA has been proven [16,17]. It is established that the basis of the mechanism of interaction of LILI with a biological object is photophysical and photochemical reactions associated with the resonant absorption of light by tissues and the violation of weak intermolecular bonds, as well as the perception and transfer of the effect of laser irradiation by liquid media in organisms [17]. Thus, the local combined application of a complex of metal nanoparticles and NILI is a promising direction in experimental surgery PLA.

### Aim of the Study

The aim of the study is to prove the effectiveness of the combined use of low-intensity laser radiation and a complex of metal nanoparticles in the surgical treatment of HAP in an experiment.

### Materials and Methods

Experimental studies on 80 laboratory rabbits of both sexes of the "white Vatican" breed weighing  $2000 \pm 50$  g and weighing from 4.8 to 5.1 kg. The research was carried out at the Department of Operative Surgery and Topographic Anatomy FGBOU VO "Saratov State Medical University named after V. I. Razumovsky" of the Ministry of Health of the Russian Federation and do not contradict the "Rules of work with the use of experimental methods animals", the Helsinki Declaration of 1975, "Rules for carrying out work using experimental animals" (adj. to the order of the Ministry of Health of the USSR of 12.08.1977 No. 755) and the European Convention for the Protection of Vertebrates Used for Experiments or for Other Scientific Purposes (ETS No. 123), Strasbourg, 18.03.1986).

The antibacterial activity of metal nanoparticles was determined by the method of double serial dilutions in meat-peptone broth in relation to standard strains *Staphylococcus aureus* FDA 209P, *Escherichia coli* ATCC 25922 (M-17) with microbial infection at a load of  $5 \times 10^5$  CFU/ml. NC solutions (zinc and copper nanoparticles with a dimension of 50 nm) and a concentration of 1 mg/ml were prepared using ultrasonic homogenization based on a 0.24% aqueous solution of the drug for intravenous administration intralipid [18].

As a source of NILI, we used a laser therapeutic device "Matrix" with a laser head CLO 4, which has an average wavelength of 630 nm, a power of 30 MW, and a constant radiation mode. a scattering head with a spherical scattering diagram; the power flow density (PCM) for a cavity with a diameter of 1.5 cm was 5 MW/cm.

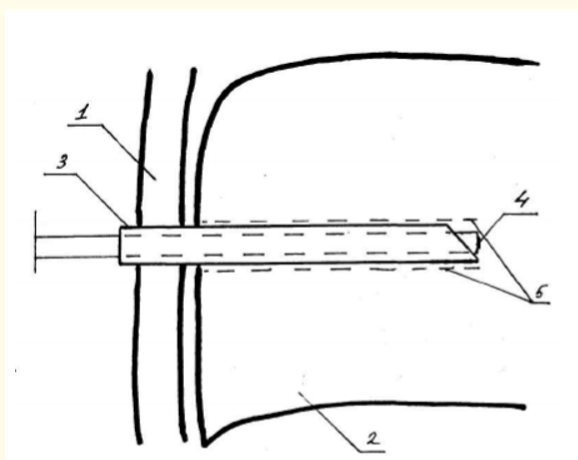
In addition, a semiconductor surgical laser device "Laser-med-1-10" with a central wavelength of 1064 nm and a power of up to 10W in constant mode. The choice of high-intensity laser irradiation generators is determined by the purpose of the study and is necessary for solving problems in an in vivo experiment. The laser radiation was transmitted through a quartz light guide with a diameter of 600 microns with a numerical aperture of 0.15. To control the spatial distribution of laser radiation, a scattering medium (0.24%) was used. an intralipid emulsion in an isotonic sodium chloride solution. A scattering head with a spherical scattering pattern was used; the power flow density (PCM) for a cavity with a diameter of 1.5 cm was 5 MW/cm. The irradiation was performed through a modified Folley-type catheter [19].

The integral quantitative assessment of the general condition of the animal was expressed in points. To create and then control the size of the PLA, an ultrasound device made in Japan, ALOKA SSD 500, was used, and MRI was performed on a Philips Achieva 1.5 T device. Radiography of the residual cavity was performed mobile X-ray machine "ARMAN 9L5". Microbiological examination was performed on the 3<sup>rd</sup>, 5<sup>th</sup>, 7<sup>th</sup>, 9<sup>th</sup>, 11<sup>th</sup> and 14<sup>th</sup> day of treatment, and the number of patients was determined. CFU of *S. aureus* in 1 ml of the contents of the abscess. Morphological examination of liver tissue biopsies was determined using a light microscope and an ocular stereometric grid. Statistical processing of the study results was carried out using the Statistica 8 and Microsoft application software package Office Excel 2007 using the Student's t-test.

Differences were interpreted as reliable when the error probability is less than 5% ( $p < 0.05$ ).

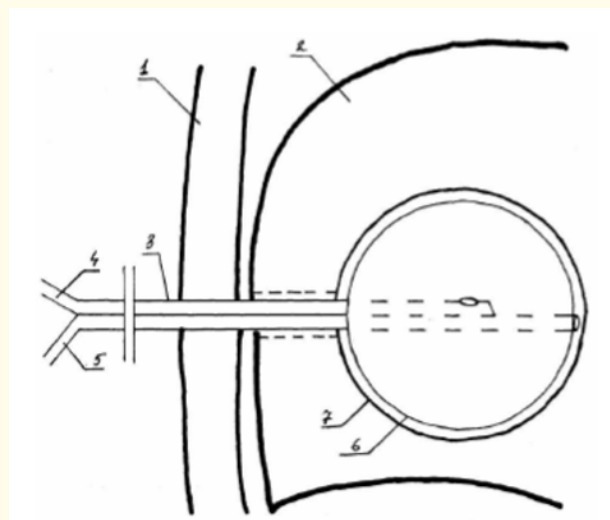
### The method of creating a PLA

The puncture method for creating a PLA was carried out according to the method developed by us [20]. Transcutaneous liver puncture was performed under the control of ultrasound with laser support [21] using a semiconductor surgical laser device "Lasarmed-1-10" with a wavelength of 1064 nm and a power of 9 watts. In the presence of laser support with a radiation power of 9 W, the puncture needle was moved into the thickness of the organ parenchyma, forming an intrahepatic channel with a depth of 20 mm (Figure 1). The laser light guide, then the needle. At the same time, in none of the observations, the outflow of blood and bile from the formed puncture channel was noted.



**Figure 1:** Diagram of the method of transcutaneous liver puncture with laser support (1- abdominal wall, 2- liver, 3 - puncture needle, 4- laser light guide, 5- intrahepatic canal).

Then, under the control of ultrasound, a modified catheter (type Foley, shortened to 3 cm) with a silicone rubber balloon infected with the above strains at the distal end. After filling and inflating the balloon with 2.0 ml of saline solution (0.9% NaCl), the catheter was ligated proximal to the balloon. After 7 days of finding the balloon in the liver parenchyma, a formed PLA cavity with a diameter of  $18 \pm 0.8$  mm ( $V=1.8$  cm<sup>3</sup>) was obtained (Figure 2).



**Figure 2:** Simulation diagram of the residual liver cavity (1- abdominal wall, 2- liver, 3- catheter, 4- first channel of the catheter, 5- second channel of the catheter, 6- balloon of the catheter in the inflated state, 7- cyst wall).

### Results and Discussion

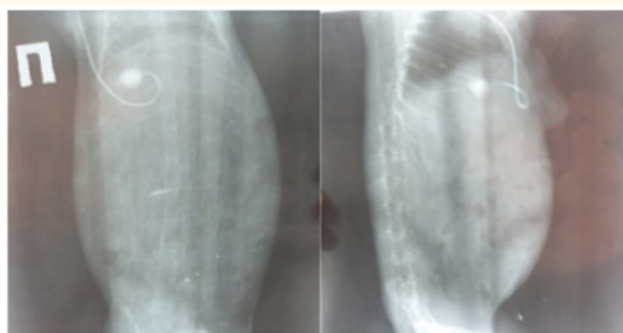
Results of treatment of PLA in animal groups. By the 20<sup>th</sup> day of treatment, the score of the general condition of the animals of the fourth group remained at the maximum figures. The value of the integral indicator of the remaining groups was lower than in the first the group was  $1.7 \pm 0,12$  in the second group and  $2.7 \pm 0,10$ , in the third group and  $2.9 \pm 0,21$  ( $p < 0.05$ ). From animals of the first and second groups, the number of CFU of strain experienced gradually decreased throughout the treatment and cleaning of the abscess cavity from pathogen from the animals of these groups were noted in only 10 days of treatment. In the third group, complete elimination of strains of microorganisms was noted on the 9<sup>th</sup> day. In the animals of the fourth group, by the 3<sup>rd</sup> day of treatment, the number of colonies decreased to  $8.62 \times 10^5$  ( $p < 0.05$ ), and by the 7<sup>th</sup> day of treatment, the cultures of aspirate from the abscess cavity did not grow. The study of experimental strains showed that metal NK in combination with NILI significantly suppressed the viability of *S. aureus* 209P and *E. coli* ATCC 25922.

On the 14<sup>th</sup> day of treatment, the minimum diameter of the abscess cavity was recorded in animals of the fourth group ( $3.5 \pm 0.6$

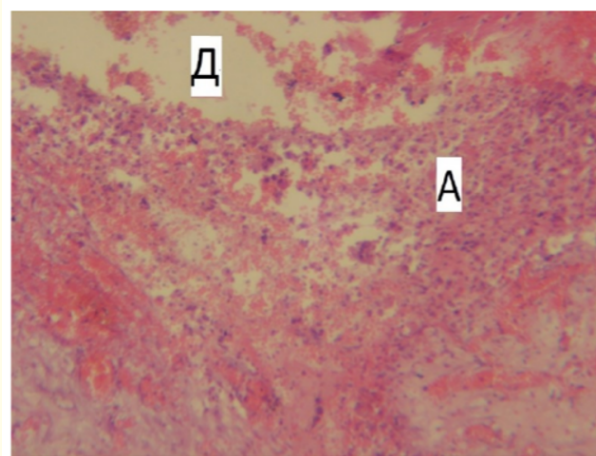
mm) ( $p < 0.05$ ), and by the 20<sup>th</sup> day of treatment, according to the data Ultrasound did not determine the gap cavity (Figure 6). Morphological studies showed that granulation tissue is attached to the cell infiltration, then a zone of loose connective tissue that passes into loose connective tissue. Just On the 20<sup>th</sup> day of treatment in animals of the fourth group, during histological examination, the abscess cavity was replaced by dense connective tissue, in the adjacent liver parenchyma there is a large area of proliferation of liver cells (Figure 7).



**Figure 3:** Ultrasound picture of rabbit liver No. 03 with simulated OP. In the parenchyma of the organ, anechoic formation of a rounded shape, with a diameter of 15 mm, wall thickness of 1 mm.



**Figure 4:** Radiographs of a rabbit with a contrasted liver cavity.  
A - Direct projection. B - Right side projection.



**Figure 5:** Preparation No. 21. A section of the rabbit liver in the border zone with a residual cavity (D) by the 5<sup>th</sup> day after the installation of a catheter with a balloon. Leukocyte infiltration, hemorrhage zones (A). Color: hematoxylin-eosin. Magnification: x 200.

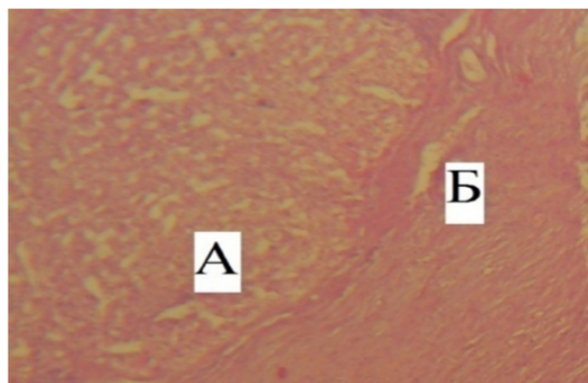


**Figure 6:** Ultrasound picture of rabbit liver No. 37 on the 20<sup>th</sup> day of treatment with a combination of NILI and nanocomplex. The cavity of the abscess is not determined.

### Discussion of the method for creating a PLA

We have identified clear clinical signs - PLA: Animals are sedentary, do not respond well to pain and sound stimuli, drink very little





**Figure 7:** Preparation No. 83. Fragment of the rabbit liver of the fourth group on the 20<sup>th</sup> day of the experiment (A- the zone of proliferation of hepatocytes, B- the growth of connective tissue at the site of the abscess cavity). Color: hematoxylin-eosin. Magnification: x 200.

water, do not eat food. It is established that the used non-invasive instrumental (ultrasound, radiography, MRI) methods of investigation are effective methods of planimetric assessment of both the liver cavity and its wall. Performing a transcutaneous liver puncture using a laser device "Lasermid-1-10" with a central wavelength of 1064 nm and a power of 9W. provides the formation of coagulation necrosis of the wall of the passed channel, providing reliable cholestasis and hemostasis.

Microbiological and morphological studies have confirmed the presence of a classic purulent liver abscess with a formed thick wall, cellular infiltration, degenerative changes and foci of necrosis at the border with the parenchyma. It was found that the puncture method of creating a PLA using a two-channel catheter with a balloon at the distal end is not traumatic, provides for the formation of a cavity with the specified characteristics in a short time, and involves the development of stable sclerosis of the liver area bordering the balloon.

#### Discussion of the results of treatment of experimental animals with PLA

A significant positive dynamics of the integral assessment of the general condition of the animals of the third and fourth groups was

established, which indicates a more favorable course of the disease. Results of treatment of animals with isolated use The NILS are comparable to the results of standard rehabilitation. The use of metal NC, which effectively suppresses the growth of pathogenic microorganisms, can act as an alternative to antibacterial drugs. Enhancing the antimicrobial effect suspensions of NK metals under the action of NILI, which simultaneously triggers the activation and self-limiting mechanisms of the inflammatory response, allows you to start treatment without determining the type of pathogen. In addition, it allows you to completely suppress pathogenic microorganisms 2 times faster than the control group, successfully stimulate reparative processes, accelerate obliteration and closure of the purulent cavity.

As a result of the use of standard PLA sanitation in the experiment (animals of the first group), the cavities were cleared of the pathogen only by the 15<sup>th</sup> - 17<sup>th</sup> day, while the size decreased only to 0.7 cm by the 20<sup>th</sup> day of treatment ( $p < 0.05$ ). Treatment of animals of the second group did not lead to the purification of the abscess cavity even by the 14<sup>th</sup> day of the experiment, with ultrasound the diameter of the cavity remained more than 0.5 cm throughout the entire observation. When treating NC metals (the third group), by the fourteenth day of treatment, the size of the abscess cavities decreased to  $0.8 \pm 0.06$  cm ( $p < 0.05$ ), depending on the pathogen of the cavity they were cleared only by the tenth day of treatment. Thus, the best results were obtained in the fourth group of animals: in the shortest possible time up to 7 days of treatment, the infected cavities are cleared of the pathogen. In the fourth group of animals, the cavity of the abscess according to ultrasound data by the tenth day of combined treatment of HAP, the size of the cavity was reduced by half, and by the 20<sup>th</sup> day of observation, the cavity was completely obliterated due to its replacement with connective tissue, and in the adjacent liver parenchyma, an extensive zone of proliferation of liver cells.

#### Conclusions

- The puncture method of creating a liver abscess using a two-channel catheter with a balloon is not traumatic, in a short time it provides the formation of an abscess cavity with the specified characteristics and is suitable for optimizing the options for its combined surgical treatment.
- The used clinical and instrumental methods of research are effective ways to evaluate the results of treatment of modulated purulent liver abscess.

- Combined surgical treatment of simulated liver abscesses with local application of evenly dispersed NILI and NK metals provides purification from the pathogen of the abscess cavity by the 7<sup>th</sup> day of treatment, achieving the maximum integral indicator of the general condition of the animal by the 9<sup>th</sup> day of treatment and complete obliteration of the abscess cavity by the 20<sup>th</sup> day of observation.

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**Volume 5 Issue 7 July 2021**

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