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PHENOMENON OF DEMIKHOV

The origin of the assisted circulation concept and its implementation (V.P. Demikhov, 1937–1947)

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Abstract

It is generally accepted that the concept of mechanical circulatory support originates from the USA in the 1960s and was implemented in the clinic by American surgeons S. Crawford, M. DeBakey, D. Cooley, D. Liotta and others by creating portable implantable pneumatic devices included in the cardiovascular system parallel to the biological heart to maintain its activity in heart failure. However, we found that twenty years earlier, in 1947, a similar concept was first put forward by the Soviet biologist and physiologist V.P. Demikhov, who had implemented it in an experiment by creating implantable electromechanical devices and transplanting a second, additional heart into the animal chest. At the

same time, V.P. Demikhov suggested using his models both for maintaining the function of a weakened biological heart and for its recovery. Since an idea similar to that published in an English-language edition had never been formulated by anyone before V.P. Demikhov, his priority is global.

Keywords: history of transplantation, mechanical circulatory support, V.P. Demikhov

Conflict of interests Authors declare no conflict of interest

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Introduction

It is known that the first experiments on the arrested heart revival were made at the beginning of the 20th century by Russian physiologists A.A. Kulyabko [1] and F.A. Andreev [2]. It is also known that the concept of artificial blood circulation (assisted circulation) to replace the function of one's own heart, as well as to work in parallel with it, was born in the USSR in the 1920s and belongs to the Soviet doctor and physiologist S.S. Bryukhonenko who created an original extracorporeal electromechanical device for these purposes in 1923-1924 [3]. The idea of parallel circulation (carotid-coronary perfusion) by means of S.S.Bryukhonenko's device was used in the 1930s by N.N. Terebinskiy in his experiments with open accesses to the atrioventricular valves of the heart [4].

As for intracorporeal implantable devices, publications about their origin and use date back to the 1960s and belong to American surgeons. In 1963, S. Crawford and D. Liotta were the first to implant an

intracorporeal pneumatic pump (Fig. 1) [5]. In 1966, M. DeBakey and D. Liotta used a paracorporeal pneumatic pump as a "bridge to recovery" due to the cardiogenic shock that developed in the patient in the early postoperative period after cardiac surgery (Fig. 2) [6]; and in 1969, D. Cooley and D. Liotta implanted a pneumatically driven artificial heart, representing two Liotta-DeBakey pumps, with the goal of further heart transplantation, that is, as a "bridge to transplantation" [7].

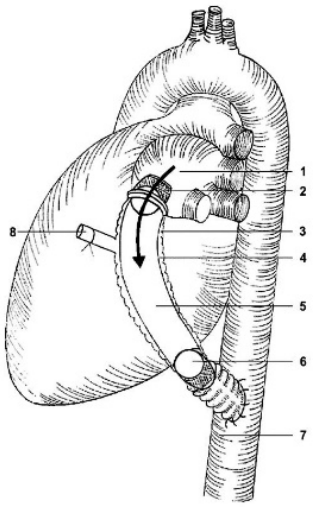


Fig. 1. Scheme of the first clinical implantation ventricle assisted device. 1963: 1 − left atrium; 2 − inlet valve; 3 − housing of Silastic, reinforced with Dacron fabric; 4 − air chamber; 5 − blood chamber; 6 − outlet valve; 7 − descending aorta; 8 − plastic tube (internal dimension, 4 mm) for air supply [5]

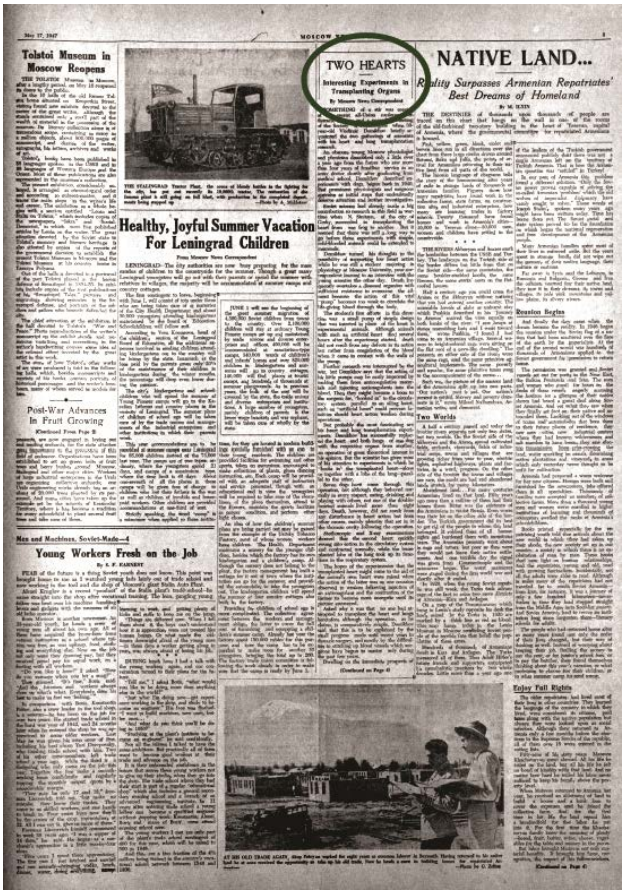
Fig. 2. A patient with a paracorporeal pneumatic ventricle. 1966 [6]

However, we believe that the world priority of the concept of a circulatory support and its practical implementation by means of orthotopic implantation of small mechanical devices, as well as of a second additional donor heart into the chest of a warm-blooded animal, belongs to the Soviet biologist and physiologist V.P. Demikhov (Fig. 3). Recall that in 1937-1938, it was V.P. Demikhov who implanted the world's first mechanical heart, and in 1946-1974, developed several dozen models of assisted circulatory support with a functioning second, additional heart to help a weakened, biological one. We described these experiments in a series of articles published in the *Transplantologiya* journal in 2013–2022. But until recently we have had no answers to the questions: “Who was the first to propose the idea of assisted circulatory support by using implantable devices? And if it was done by V.P. Demikhov, when did this happen?

Fig. 3. V.P. Demikhov is auscultating the chest of a dog with two hearts. 1950s

The answer came after a content analysis of an item entitled “Two hearts. Interesting Experiments in Transplanting Organs”, published in

"The Moscow New" issue of May 17, 1947 (Fig. 4) [8]. It follows from the text that it was V.P. Demikhov who in 1947 for the first time in the world formulated the modern concept of assisted circulatory support, put forward the idea of creating mechanical devices to bypass the left heart and implemented it in a biological version. We have translated the text of this note into Russian and in this article we introduce it into scientific circulation for the first time.



Tolstoi Museum in Moscow Reopens

TWO HEARTS
Interesting Experiments in Transplanting Organs

NATIVE LAND...
Reality Surpasses Armenian Repatriates' Best Dreams of Homeland

Healthy, Joyful Summer Vacation For Leningrad Children

Post-War Advances In Fruit Growing

Young Workers Fresh on the Job

Fig. 4. Item in “The Moscow News” paper dated May 17, 1947

"TWO HEARTS. Interesting experiments on organ transplantation from the reporter of "The Moscow News"

Something of a stir was caused by the recent All-Union Conference on Thoracic Surgery and the previous meeting of the Physiological Society, when thirty-year-old Vladimir Demikhov briefly presented his research in the field of heart and lung transplantation to two meetings of scientists. A little-known young Moscow physiologist and doctor,

> demobilized a little over a year ago from the Armed Forces, who soon after graduating from medical school spent more than four years of front-line service as an army doctor, Demikhov described experiments with dogs that he started back in 1940, appreciated by outstanding physiologists and surgeons as initial steps, which undoubtedly deserve attention and further study" [8].

The beginning of this newspaper item needs some explanation. The fact is that the presentation by V.P. Demikhov, an Assistant of the Pathological Physiology Department of the Moscow Fur Institute in spring, 1947, at the Meeting of the Moscow Scientific Society of Physiologists [1], and then at the 1st All-Union Conference on Thoracic Surgery, caused an ambiguous response from the audience. On the one hand, a 31-year-old physiologist and pathologist (by military specialty) actually made unusual for that time presentations on homologous heart and lung transplantation in dogs. But, on the other hand, it was not a spontaneous, but a deeply thought-out performance. Since V.P. Demikhov invented his first implantable mechanical heart in 1937–1938, and the transplantation of a second, additional heart to animals on the vessels of the neck became the topic of his thesis on his graduation from the Biological Faculty of M.V. Lomonosov Moscow State University in 1940 with the degree in Human and Animal Physiology.

The following words of the item indicate that "The Moscow News" reporter was familiar with the state of experiments in the field of heart transplantation in the USSR, because then the discussion turned to investigations by N.P. Sinitsyn, a pharmacologist from the Gorky Medical Institute.

[1]There is evidence that at the same period of time V.P. Demikhov also spoke at a Meeting of the Moscow Scientific Society of Pathophysiologists. It is possible that this was a Joint Meeting of the two Societies.

> “Soviet science has already made a great contribution to research in this area in wartime, when N. Sinitsyn from the city of Gorky managed to transplant a heart from one frog to another. But it seemed that there was still a long way to go before these experiments with simple cold-blooded animals could be extended to mammals” [8].

Indeed, in the second half of the 1930s, for the first time in the world, N.P. Sinitsyn began to transplant the heart of frogs orthotopically, into the chest cavity, in order to study the neurohumoral effect of certain medicinal substances on the myocardium. Most likely, V.P. Demikhov told the reporter about those experiments. But V.P. Demikhov obviously missed the article published by N.P. Sinitsyn in 1942 about transplanting a second heart into a dog. We mention this to emphasize that he was not alone in his research. Note, however, that N.P. Sinitsyn conducted his experiments with a pharmacological purpose rather than with a physiological one [9].

In essence, this is a prehistory to what is discussed below.

The origination of the intracorporeal assisted circulatory support concept and the attempt of its implementation by implanting mechanical pumps

> “In an interview with our correspondent these days, a young scientist (V.P. Demikhov. - *Ed.*) reported that he thought about the possibility of ***supporting the function of a weakened heart*** (hereinafter, in direct speech, it is highlighted by us. - *Auth.*), specializing in physiology at Moscow University. Because the action of this vital pump becomes too weak to keep the blood circulating in the body, death often overtakes the diseased body, which has enough resistance to overcome the disease.
>
> The student's first efforts in this direction were the creation of a small pump of a simple design, which was implanted instead of a heart in

experimental animals. Although animals with such an artificial heart died a few hours after the start of the experiment, the cause of death was not any errors in the operation of the pump, but clotting of the blood that was in contact with its walls.

Further research was interrupted by the war, but Demikhov says his small pumps could easily be improved by making them from anticoagulant-coated materials or by injecting anticoagulants into the bloodstream. If such pumps are ***included in the circulatory system parallel to the diseased heart*** , then such an artificial heart could prevent malfunctions of the [sick] heart if it is weakened during surgical operations" [8].

It is at this point in the text that we are talking about the birth of the assisted circulation idea. V.P. Demikhov made his initial 3 experiments in the replacement of the biological heart with an implantable electromechanical pump equal to it in size in Voronezh in 1937–1938. In the last experiment, a dog with a mechanical heart lived for 2.5 hours, after which the experiment was interrupted "for technical reasons". These experiments were first described by a reporter of a large-circulation newspaper of the Voronezh State University, where V.P. Demikhov studied in 1934–1938. In 1951, Issue 7 of the Bulletin of Experimental Biology and Medicine journal, published an article entitled "Experimental grounds for replacing the heart with a mechanical device in an acute experiment" (with a footnote: "Reported at a Scientific Students' Conference of Voronezh State University in April 1938"), where the "scheme for replacing the heart with a mechanical device" was first presented (Fig. 5) [10].

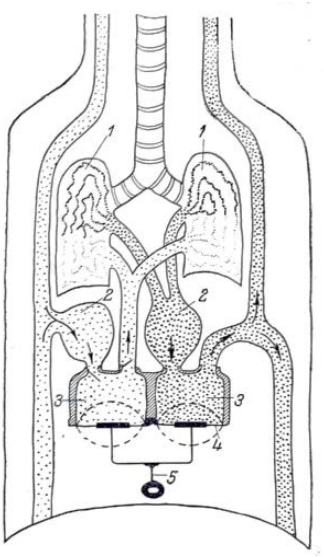


Fig. 5. Scheme for replacing the heart with a mechanical assist device: 1 – lungs, 2 – atria of the removed heart, 3 – cavities of the device replacing the cavities of the heart ventricles, 4 – rubber membrane of the device, 5 – the rod moving the membranes. The device was created in 1937; the scheme was published in 1951 [10]

In summer of 1938, after V.P. Demikhov's move to Moscow, he designed several more models of a mechanical heart, which he reported in 1959 by re-publishing the scheme of orthotopic implantation of a mechanical heart [11], and later, in 1960, in his book “Experimental Transplantation of Vital Organs” [12], but without the scheme. Note, however, that those V.P. Demikhov's experiments were to replace the biological heart with a mechanical pump, and in an interview with “The Moscow News” reporter he talked about the parallel inclusion of such pumps in the blood circulation system. As known, in the following years V.P. Demikhov did not create implanted any more mechanical pumps to bypass the left heart, limiting himself to the idea he put forward and the creation of pumps (artificial hearts) for replacement circulation, although he repeatedly emphasized the fact that the “devices and methods known to him for maintaining artificial circulation of a whole body during a cardiac arrest (Andreev, Bryukhonenko, Negovsky, Geimans and others)

<...> support artificial circulation while maintaining a natural heart in the body” [10].

So, we have shown that the *idea of using implantable "small" mechanical pumps made of materials with anticoagulant properties and included in the circulatory system parallel to the sick, weakened heart to maintain its function, including during operations, belongs to V.P. Demikhov.* The origin of this idea dates back to 1937, and it was formulated in 1947.

The origination and implementation of the intracorporeal assisted circulatory support concept by transplantation of an additional heart

> “But probably the most exciting are his (V.P. Demikhov. - *Ed.*) experiments on heart and lung transplantation. Demikhov successfully replaced the heart and both lungs of one dog with the corresponding organs of another, which, in his opinion, is of great theoretical interest" [8].

Here is another world priority of V.P. Demikhov to be talked about, namely, the experimental transplantation of the cardiopulmonary complex, which in 1947, in his opinion, was of "great theoretical interest" only. And then comes the most important part.

> “But the scientist devoted most of his attention to experiments in which he connects a transplanted heart - separately or together with a lobe of the lung - ***in parallel to another***. Seven operated dogs survived the operation normally, eating, drinking and playing with others, but none of the animals with a transplanted heart survived more than 8 days. Death, however, did not occur as a result of any disturbances in cardiac activity, but from other causes, mainly from pleurisy that arose after the operation.
>
> Stethoscopic and X-ray studies showed that the second heart quickly joined the circulatory system and contracted normally, while the

transplanted lobe of the lung performed its functions in the respiratory system. The hopes of the experimenter that the ***transplanted heart could come to the aid of the animal*** 's own heart were justified when it was once noticed that the action of the latter weakened after an injection of an anticoagulant, and the contraction of the former became more vigorous until the latter stabilized" [8].

In this part of the item, V.P. Demikhov says that assisted blood circulation can be provided by transplanting a second, additional heart into the chest cavity of a warm-blooded animal, and this second heart would work in parallel with the weakened native heart. It was the scheme that he developed over the years, having come up with more than two dozen variants of it (Fig. 6).

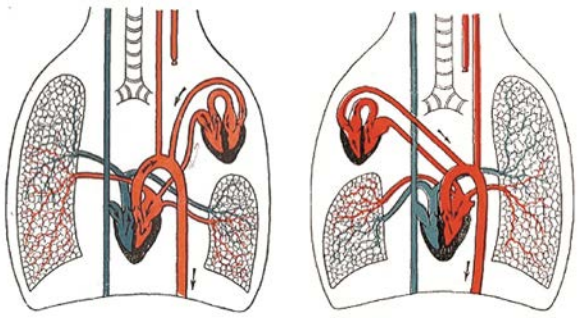


Fig. 6. Schemes No. 9 (left) and No. 14 (right) of transplanting a second, additional heart into the dog's chest to maintain the function of the biological heart. 1960 [12]

In this part of the article, we have demonstrated that the *idea of using a second, additional donor heart as a kind of "implantable biological pump" included in the circulatory system parallel to the weakened native heart to maintain its function also belongs to V.P. Demikhov.* The origin of this idea dates back to 1946, and it was also formulated in 1947.

> “When asked why, until now, no one has been tempted to transplant a heart and lungs, although the operation, as he claims, is relatively simple, Demikhov said that this is due to the small progress made in recent years in chest surgery, and mainly because for the difficulties with suturing blood vessels, which surgeons have only recently begun to master.
>
> Returning to his research, the scientist said: “I must first improve the surgical technique and postoperative treatment so that dogs live longer, so that we can study the function of a transplanted heart in months, not days. My second goal, Demikhov said in conclusion, is to prove the possibility of transplanting preserved organs. The prospects this opens up are obvious. I am almost certain that transplantation of a preserved heart should be as possible as transplantation of a preserved vessel wall. Soviet scientists S. Andreev and N. Osinovsky restored cardiac activity many hours (up to 99) after death, so there is every hope of success. As for the further prospects for the development of my method, it is still too early to comment on anything. The experimenter has every right to indulge in flights of fantasy, but he has no right to talk about them until they become a reality” [8].

From the text of the final part of the newspaper item, we learn that V.P. Demikhov saw the main difficulties of experimental heart and lung transplantation in 1947 in a poor development of thoracic surgery and the need to improve the technique of suturing blood vessels in an end-to-end manner. Indeed, the first pneumonectomy operations were performed in the USSR in 1946 [13], and the first operation on the ligation of the patent ductus arteriosus was performed by A.N. Bakulev only in 1948 [14]. At the same time, a simple, airtight and high-quality circular vascular suture was implemented in surgical practice (with the participation of V.P. Demikhov) by using V.F. Gudov's vascular stapling device (Fig. 7) [15]. Recall that in 1947 V.P. Demikhov spoke about the

need to use anticoagulants for the thrombosis prevention while implementing the assisted circulatory support.

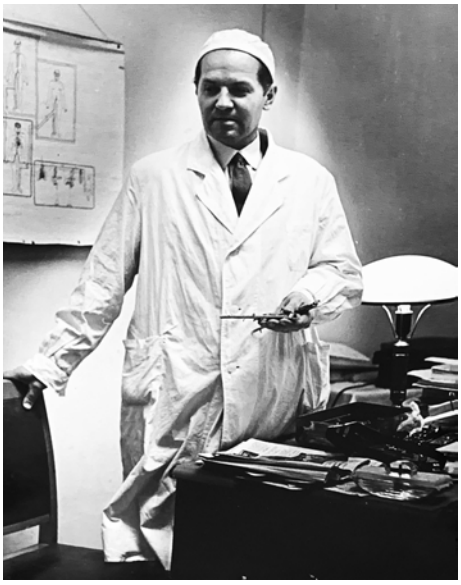
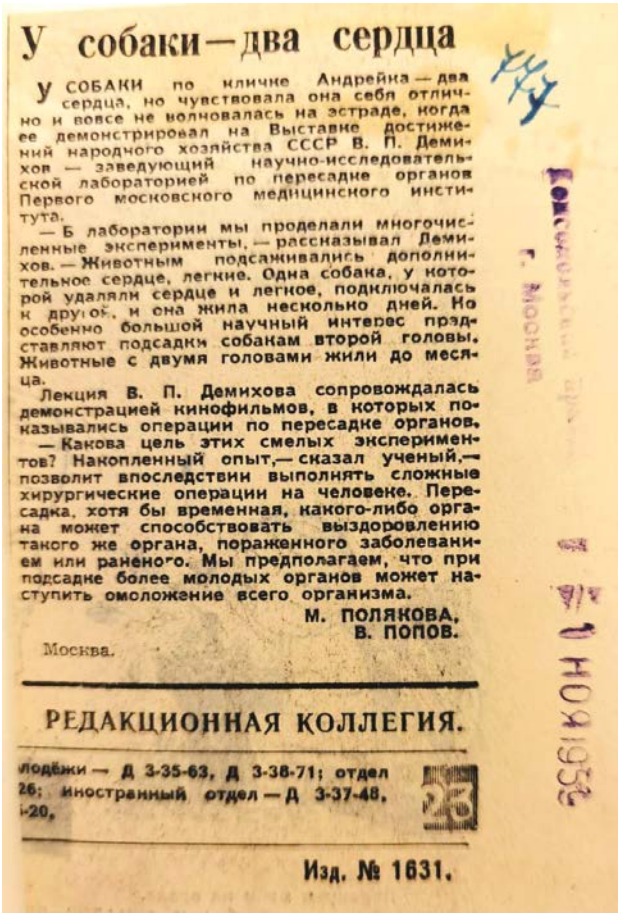


Fig. 7. V.P. Demikhov is holding V.F. Gudov's vascular stapling device in hands

It was as early as in the 1950s when V.P. Demikhov mentioned that by transplanting an additional heart, it was possible to maintain the function of a sick biological heart until its recovery; that had been long before the Americans voiced this concept (a bridge to recovery) in 1966. To prove this assertion, let us cite an article from the *Komsomolskaya Pravda* newspaper dated November 1, 1959, and entitled “A dog has two hearts” (Fig. 8).



У собаки — два сердца

У СОБАКИ по кличке Андрейка — два сердца, но чувствовала она себя отлично и вовсе не волновалась на эстраде, когда ее демонстрировал на Выставке достижений народного хозяйства СССР В. П. Демихов — заведующий научно-исследовательской лабораторией по пересадке органов Первого московского медицинского института.

— В лаборатории мы проделали многочисленные эксперименты, — рассказывал Демихов. — Животным подсаживались дополнительное сердце, легкие. Одна собака, у которой удаляли сердце и легкое, подключалась к другой, и она жила несколько дней. Но особенно большой научный интерес представляют подсадки собакам второй головы. Животные с двумя головами жили до месяца.

Лекция В. П. Демихова сопровождалась демонстрацией кинофильмов, в которых показывались операции по пересадке органов.

— Какова цель этих смелых экспериментов? Накопленный опыт, — сказал ученый, — позволит впоследствии выполнять сложные хирургические операции на человеке. Пересадка, хотя бы временная, какого-либо органа может способствовать выздоровлению такого же органа, пораженного заболеванием или раненого. Мы предполагаем, что при подсадке более молодых органов может наступить омоложение всего организма.

М. ПОЛЯКОВА,
В. ПОПОВ.

Москва.

РЕДАКЦИОННАЯ КОЛЛЕГИЯ.

лодёжи — Д 3-35-63, Д 3-38-71; отдел 26; иностранный отдел — Д 3-37-48, і-20,

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Fig. 8. Item in the "Komsomolskaya Pravda" newspaper dated November 1, 1959

In particular, it says that in autumn of 1959, at the Exhibition of the USSR National Economy Achievements in Moscow, V.P. Demikhov showed a dog with two hearts, which "felt great and did not worry at all on the stage when it was demonstrated." Answering the question: "What is the purpose of these experiments?" V.P. Demikhov said:

> "The experience gained will allow us to subsequently perform complex surgical operations on humans. ***Transplantation, even if temporary, of any organ can contribute to the recovery of the similar organ, affected by a disease or wounded***" [16].

Conclusion

After 1947 V.P. Demikhov created more advanced models of an additional heart, having achieved the maximum term of a transplanted organ survival (142 days) in 1962; in 1963, he formulated the idea of a two-stage transplantation of an additional heart in a human; in 1967, he became a witness of the world's first clinical orthotopic heart transplantation performed in South Africa; from 1963 to 1969, he promoted his methodology for creating a bank of living organs for their subsequent transplantation, which had never been implemented in the clinic due to technical and ethical problems. But his fantastic goal expressed by him in 1947 and consisting in "proving the feasibility of transplanting preserved organs" was achieved, although without his participation. Today, transplantations of heart, lung, and other organs have become routine. And this is a great significance of V.P. Demikhov's work as a scientist.

However, in this article we are talking about another world priority of V.P. Demikhov. V.P. Demikhov saw one of the ways to prolong the function of a sick heart before transplantation or until recovery in the use of implantable mechanical pumps or the transplantation of a second, additional heart into the human chest. Such electromechanical and pneumatic devices presented in the USA in the 1960s as "a bridge to transplantation" of the heart and "a bridge to recovery" have become widely used since the 1980s for long-term treatment of heart failure (destination therapy), and also as "a bridge to decision making".

The documents we have found allow us to assert that this concept, both in mechanical and biological variants, is also owing to the outstanding Soviet and Russian scientist V.P. Demikhov for its birth and experimental implementation.

Thus, based on the above, we argue that the concept of assisted circulation using both implantable mechanical devices and a second, additional heart was developed and implemented by V.P. Demikhov in 1937–1947, and first reported by him in 1947. Taking into account the fact that this idea was formulated and implemented abroad much later, the world priority for the creation and implementation of the concept of assisted circulation support belongs to V.P. Demikhov.

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